AGENCE NATIONALE DU
MEDICAMENT VETERINAIRE

Agence nationale du médicament vétérinaire (ANMV)
French agency for veterinary medicinal products

AGENCE NATIONALE DE SÉCURITÉ SANITAIRE de l'alimentation, de l'environnement et du travail
FRENCH AGENCY FOR FOOD, ENVIRONMENTAL AND OCCUPATIONAL HEALTH AND SAFETY
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PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Remuvet 40 mg/200 mg spot-on solution for dogs up to 4 kg
Remuvet 100 mg/500 mg spot-on solution for dogs over 4 kg and up to 10 kg
Remuvet 250 mg/1250 mg spot-on solution for dogs over 10 kg & up to 25 kg
Remuvet 400 mg/2000 mg spot-on solution for dogs over 25 kg & up to 40 kg

24 October 2023

PRODUCT SUMMARY

EU procedure number	FR/V/0440/001-004/DC
Name, strength and pharmaceutical form	Remuvet 40 mg/200 mg spot-on solution for dogs up to 4 kg. Remuvet 100 mg/500 mg spot-on solution for dogs over 4 kg up to 10 kg. Remuvet 250 mg/1250 mg spot-on solution for dogs over 10 kg up to 25 kg. Remuvet 400 mg/2000 mg spot-on solution for dogs over 25 kg up to 40 kg.
Applicant	BEAPHAR B.V. DROSTENKAMP 3 8101BX RAALTE, THE NETHERLANDS
Active substance(s)	Imidacloprid Permethrin
ATC vetcode	QP53AC54
Target species	Dogs
Indication for use	For the treatment and prevention of flea (*Ctenocephalides canis*, *Ctenocephalides felis*) infestation. Fleas on dogs are killed within one day following treatment. One treatment prevents further flea infestation for four weeks. The veterinary medicinal product can be used as a part of a treatment strategy for flea allergy dermatitis. The veterinary medicinal product has persistent acaricidal and repellent efficacy against tick infestations (*Rhipicephalus sanguineus* and *Ixodes ricinus* for four weeks, and *Dermacentor reticulatus* for three weeks). By repelling and killing the tick vector *Rhipicephalus sanguineus,* the veterinary medicinal product reduces the likelihood of transmission of the pathogen *Ehrlichia canis,* thereby reducing the risk of canine ehrlichiosis. The reduction in risk has been shown in studies to commence from 3 days following application of the veterinary medicinal product and to persist for 4 weeks. Ticks already on the dog may not be killed within two days after treatment and may remain attached and visible. Therefore the removal of ticks already on the dog at the time of treatment is recommended, in order to prevent them from attaching and having a blood meal. For the treatment of biting lice (*Trichodectes canis*).

	One treatment provides repellent (anti-feeding) activity against: - sand flies (*Phlebotomus papatasi* for two weeks and *Phlebotomus perniciosus* for three weeks), - mosquitoes (*Aedes aegypti* for two weeks and *Culex pipiens* for four weeks) - stable flies (*Stomoxys calcitrans*) for four weeks. Reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*) for up to 3 weeks. The effect is indirect due to veterinary medicinal product's activity against the vector.

Remuvet (Preventix) spot-on solution for dogs	FR/V/0440/001-004/DC
Beaphar B.V.	DCP
Publicly available assessment report	

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 13(3) of Directive 2001/82/EC as amended.
Reference product (RP)	Advantix Spot-on solution for dogs up to 4 kg Advantix Spot-on solution for dogs over 4 kg up to 10 kg Advantix Spot-on solution for dogs over 10 kg up to 25 kg Advantix Spot-on solution for dogs over 25 kg up to 40 kg
Marketing authorisation holder	Elanco
Marketing authorisation number EU procedure number	FR/V/1324410 9/2004, FR/V/2857504 9/2004, FR/V/0721081 9/2004, FR/V/7763031 7/2004 IT/V/0113/001, IT/V/0114/001, IT/V/0115/001, IT/V/0116/001
Date of authorisation	27/01/2004
Date of completion of the original decentralised procedure	20/09/2023
Concerned Member States for original procedure	CY, CZ, DE, EL, ES, HR, HU, IT, LT, LV, MT, NL, PL, PT, RO, SI, SK
Withdrawn CMS during original decentralised procedure	The company decided to withdraw the application in Estonia (EE). At the time of withdrawal, the MS considered that the data provided could allow to conclude on a positive benefit-risk balance if the points for clarification were solved.

*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 referenceability 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

A. Product description

The VMP contains 500 mg permethrin cis/trans 40/60 and 100 mg imidacloprid as active substances per mL of solution and the excipients butylhydroxytoluene (10 mg/mL) used as antioxidant, N-methyl-2-pyrrolidone (468 mg/mL), miglyol and citric acid.

The VMP is filled in white polypropylene pipette of 0.4 mL, 1.0 mL, 2.5 mL or 4.0 mL, depending on the weight of dogs to be treated. Each pipette is packed in a multi-layered polyethylene terephthalate – polyethylene – aluminium foil – surlyn sachet. The sachets are packed into a cardboard box, containing either 1, 2, 3, 4, 6, 12 or 24 unit dose pipettes.

The formulation, the choice of the excipients and presence of antioxidant are 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 licensed manufacturing sites.

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

C. Production and control of starting materials

The VMP contains two active substances. The active substances are Imidacloprid, an established substance described in the European Pharmacopeia, and (RS)-Permethrin cis: trans 40:60, an established active substance. 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.

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 sites 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

This application for marketing authorisation is being made according to the provisions of Article 13(3) of Directive 2001/82/EC as amended by Directive 2004/28/EC. The reference veterinary medicinal product is Advantix, marketed by ELANCO, which has been authorized in European Union since 27/01/2004.

Warnings and precautions as listed in the product literature are in line with those of the reference VMP and have been updated with the latest insights. They are adequate to ensure safety of the product to users, the environment and the consumers.

A. Safety tests

Pharmacological studies

As this is a hybrid application according to Article 13(3) of Directive 2001/82/EC as amended and essential similarity to a reference VMP has been demonstrated, results of pharmacological tests are not required.

Toxicological studies

As this is a hybrid application according to Article 13(3) of Directive 2001/82/EC as amended and essential similarity to a reference VMP has been demonstrated, results of toxicological tests are not required.

However, for this hybrid application, bibliographic information on the toxicological effects of active substances and excipients has been provided.

User safety

The applicant has provided a user risk assessment in compliance with the relevant guidelines In order to refine the assessment and to evaluate the potential residues of active substances and the excipient NMP towards which the user and a child might be exposed following the use of the product, a wipe study has been performed.

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 veterinary medicinal product will only be used in non-food animals.

Given that this veterinary medicinal product is an ectoparasiticide applied topically to dogs, a recommendation for dogs not entering watercourses for two days after application has been included.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a hybrid application according to Article 13(3) of Directive 2001/82/EC as amended and essential similarity to a reference VMP has been demonstrated, efficacy studies are not required.

A. Pre-Clinical Studies

Pharmacology

No pharmacological pre-clinical studies were performed.

Development of resistance and related risk in animals

A literature review of current published information concerning resistance to imidacloprid and permethrin has been performed. Adequate warnings and precautions appear on the product literature. This also includes up to date information on the resistance to actives substances in the indicated parasites.

Tolerance in the target species of animals

As this is a hybrid application according to Article 13(3) of Directive 2001/82/EC as amended, results of tolerance studies in the target species dogs are not required.
The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

As this is a hybrid application according to 13(3) of Directive 2001/82/EC as amended and bioequivalence with a reference VMP has been demonstrated, clinical trials are not required.

The efficacy claims for this VMP are equivalent to those of the reference VMP.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

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