AGENCE NATIONALE DU

MEDICAMENT VETERINAIRE

FRENCH AGENCY FOR FOOD, ENVIRONNEMENTAL AND OCCUPATIONAL HEALTH SAFETY

FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

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PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

FLEAGUARD PLUS

PRODUCT SUMMARY

EU procedure number	FR/V/0498/001-005/DC
Name, strength and pharmaceutical form	Fleaguard Plus 40 mg/200 mg Spot-on Solution for Dogs up to 4 kg Fleaguard Plus 100 mg/500 mg Spot-on Solution for Dogs over 4 kg up to 10 kg Fleaguard Plus 250 mg/1250 mg Spot-on Solution for Dogs over 10 kg up to 25 kg Fleaguard Plus 400 mg/2000 mg Spot-on Solution for Dogs over 25 kg up to 40 kg Fleaguard Plus 600 mg/3000 mg Spot-on Solution for Dogs over 40 kg up to 60 kg
Applicant	CHANELLE PHARMACEUTICALS MANUFACTURING LIMITED DUBLIN ROAD, LOUGHREA – - CO. GALWAY – IRLANDE
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 product can be used as part of a treatment strategy for flea allergy dermatitis (FAD). For the treatment of biting lice (*Trichodectes canis*). The product has persistent acaricidal and repellent efficacy against tick infestations (*Rhipicephalus sanguineus* and *Ixodes Ricinus* for four weeks, and *Dermacentor recticulatus* for three weeks). By repelling and killing the tick vector *Rhipicephalus sanguineus*, the 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 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. One treatment provides repellent (anti-feeding) activity against sand flies (*Phlebotomus papatasi* for two weeks and *Phlebotomus pernicious* for three weeks), against mosquitoes (*Aedes aegypti* for

	two weeks and *Culex pipiens* for four weeks) and against 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 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 Regulation (EC) 2019/6 as amended.
Reference product (RP)	ADVANTIX TRES PETIT CHIEN
Marketing authorisation holder	ELANCO
Marketing authorisation number EU procedure number	IT/V/0113/001/MR
Date of authorisation	27/01/2004

Legal basis of original application*	Hybrid application in accordance with Regulation (EC) 2019/6 as amended.
Reference product (RP)	ADVANTIX PETIT CHIEN
Marketing authorisation holder	ELANCO
Marketing authorisation number EU procedure number	IT/V/0114/001/MR
Date of authorisation	27/01/2004

Legal basis of original application*	Hybrid application in accordance with Regulation (EC) 2019/6 as amended.
Reference product (RP)	ADVANTIX CHIEN MOYEN
Marketing authorisation holder	ELANCO
Marketing authorisation number EU procedure number	IT/V/0115/001/MR
Date of authorisation	27/01/2004

Legal basis of original application*	Hybrid application in accordance with Regulation (EC) 2019/6 as amended.
Reference product (RP)	ADVANTIX GRAND CHIEN
Marketing authorisation holder	ELANCO
Marketing authorisation number EU procedure number	IT/V/0116/001/MR
Date of authorisation	27/01/2004

Legal basis of original application*	Hybrid application in accordance with Regulation (EC) 2019/6 as amended.
Reference product (RP)	ADVANTIX TRES GRAND CHIEN
Marketing authorisation holder	ELANCO
Marketing authorisation number EU procedure number	IT/V/0113/002/DX/001
Date of authorisation	31/10/2017

*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 (physicochemical, biological or microbiological information)

A. Product description

The VMP contains 100 mg of imidacloprid and 500 mg of permethrin cis/trans 40/60 by mL of solution and the excipients butylhydoxytoluene (E321), citric acid, triglycerides, medium chain and N-methylpyrrolidone.

The VMP is filled in multilayer polypropylene pipette of 0.4 mL, 1.0 mL, 2.5 mL, 4.0 mL of 6.0 mL with snap-off cap, depending on the weight of dogs to be treated. Each pipette is packed in a multi-layered polyethylene terephthalate/aluminium foil/oPA/LLDPE child-resistant sachet. The sachets are packed into a cardboard box, containing either 1, 2, 3, 4, 6 or 24 unit dose pipettes.

The choice of the formulation and the 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.

Process validation data on the VMP have been presented in accordance with the relevant European guidelines and will be completed post-authorisation on the maximum batch size.

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.

Scientific data and certificate of suitability issued by the EDQM 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.

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.

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 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 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 essential similarity to a reference VMP has been demonstrated, results of safety tests are not required

A. Safety tests

Pharmacological studies

See part IV.

User safety

The applicant has provided a user safety assessment in compliance with the Guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.1. 15 March 2010) and the CVMP Guideline on user safety of topically administered veterinary medicinal products (EMA/CVMP/SWP/721059/2014).

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

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

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.

However, the following RMMS are included in the SPC, and product literature:

“Imidacloprid and Permethrin are toxic for aquatic organisms. Treated dogs should not be allowed to enter surface water for 48 hour after treatment, to avoid adverse effects on aquatic organisms.”

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and essential similarity to a reference VMP has been demonstrated, efficacy studies are not required.

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

A. Pre-Clinical Studies

No pre-clinical studies were performed.

Development of resistance and related risk in animals

The bibliography / information provided suggests that resistance to permethrin in fleas, ticks (*Rhipicephalus sanguineus*), stable flies (*Stomoxys calcitrans),* mosquitoes (*Culex pipiens, Aedes aegypti*) and sandflies (*Phlebotomus papatasi*) exist.

Adequate warnings and precautions appear on the product literature.

Dose determination and confirmation

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and essential similarity to a reference VMP has been demonstrated, dose determination and confirmation studies are not required.

Tolerance in the target species of animals

This is an application submitted in accordance with article 19(1) of Regulation (EU) 2019/6 and essential similarity with the reference product has been established it is accepted that the tolerance of the candidate product will be similar to those of the reference product.

B. Clinical trials

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and essential similarity to a reference VMP has been demonstrated, results of 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.