Austrian
Federal Office for
Safety in Healthcare
BASG

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Frento Forte 40 mg Spot-on Solution for Small Dogs
Frento Forte 100 mg Spot-on Solution for Medium Dogs
Frento Forte 250 mg Spot-on Solution for Large Dogs
Frento Forte 400 mg Spot-on Solution for Extra Large Dogs

AT/V/0023/001-4/DC
(Former: UK/V/0662/001-4/DC)

Date: July 2018
Last update: 03/08/2021

Modules 1-3 reflect the scientific discussion for the approval of Frento Forte. The procedure was finalised on 31/05/2018. For information on changes after this date please refer to module 4.

MODULE 1

PRODUCT SUMMARY

EU Procedure numbers	AT/V/0023/001/DC AT/V/0023/002/DC AT/V/0023/003/DC AT/V/0023/004/DC
Name, strength and pharmaceutical form	Frento Forte 40 mg Spot-on Solution for Small Dogs Frento Forte 100 mg Spot-on Solution for Medium Dogs Frento Forte 250 mg Spot-on Solution for Large Dogs Frento Forte 400 mg Spot-on Solution for Extra Large Dogs
Applicant	Bayer Austria GmbH Herbststr. 6-10 1160 Vienna Austria
Active substance(s)	Imidacloprid
ATC Vetcode	QP53AX17
Target species	Dogs
Indication for use	For the prevention and treatment of flea infestation. For the treatment of biting lice (*Trichodectes canis*) where this has been previously diagnosed by a veterinary surgeon. Fleas 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 the control of Flea Allergy Dermatitis (FAD) where this has been previously diagnosed by a veterinary surgeon.

MODULE 2

The Summary of Product Characteristics (SPCs) for these products are available on the Product Information Database of the Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	A generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedure.	31st May 2018
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	Austria

I. SCIENTIFIC OVERVIEW

These are generic applications submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended by 2004/28/EC. The reference products are the corresponding strength Advantage spot-on solution for dogs which have been authorised in the UK since 1997 and 1999. Bioequivalence is accepted in accordance with section 7.1(d) of the current Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2). The applicant stated that the composition, specifications, test methods of the active substance and excipients, sources of the active substance and excipients, manufacturing process and manufacturer of the products are identical to those of the reference product. This was accepted.

Frento Forte Spot-on Solutions contain 40 mg per pipette, 100 mg per pipette, 250 mg per pipette and 400 mg per pipette imidacloprid for the different strengths of product.
The proposed indications for all products are:

For the prevention and treatment of flea infestations and treatment of biting lice (Trichodectes canis) on dogs of less than 4 kg body weight, on dogs of 4 kg up to less than 10 kg body weight, on dogs of 10 kg up to less than 25 kg body weight and on dogs of 25 kg body weight and greater, respectively.
Fleas 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 the control of Flea Allergy Dermatitis (FAD) where this has been previously diagnosed by a veterinary surgeon.

The proposed dosage and treatment schedules are:

Dog (kg bw)	Product	Number of Pipettes
Less than 4 kg	Frento Forte 40 mg Spot-on Solution for Small Dogs	1 x 0.4 ml
4 to less than 10 kg	Frento Forte 100 mg Spot-on Solution for Medium Dogs	1 x 1.0 ml
10 to less than 25 kg	Frento Forte 250 mg Spot-on Solution for Large Dogs	1 x 2.5 ml

25 to less than 40 kg	Frento Forte 400 mg Spot-on Solution for Extra Large Dogs	1 x 4.0 ml
40 kg and greater	Frento Forte 400 mg Spot-on Solution for Extra Large Dogs	2 x 4.0 ml

All dogs should receive a minimum dose of 10 mg Imidacloprid/kg bodyweight.

The product is 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 product can be safely used in the target species, any reactions observed are indicated in the SPC.[1] 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[2] of the product 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 CONSTIUENTS

II.A. Composition

The products contain imidacloprid at varying concentrations, and the excipients benzyl alcohol, propylene carbonate and butylhydroxytoluene.
The container/closure system consists of white polypropylene plastic tubes (pipettes) with an integrated seal membrane and polypropylene cap. 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 products are manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. Process validation data on the products have been presented in accordance with the relevant European guidelines. The manufacturing method consists of mixing in each of the ingredients, filtering and then filling.

II.C. Control of Starting Materials

The active substance is imidacloprid, an established active substance, which 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.

II.C.4. Substances of Biological Origin

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

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

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

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided. The immediate product can be stored for up to 6 months.

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 include those for clarity, colour, relative density and an additional test for refractive index, which serves to confirm that the formulation comprises the active substance and excipients in the proposed proportions.

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.
Three production scale batches were stored at 25°C/60% RH and 40°C/75%RH for up to five years and one year respectively. The results show that imidacloprid is very stable and the data support a retest period for the material of 2 years with no special storage conditions.

II.G. Other Information

This veterinary medicinal product does not require any special storage conditions. Keep the blister in the outer carton.
Shelf life of the veterinary medicinal product as packaged for sale: 5 years.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As these were generic applications according to Article 3(1) of Directive 2001/82/EC and bioequivalence with a reference product has been established, results of safety and residues tests were not required.

User Safety

A user risk assessment was not submitted with these applications, because the products are identical to the reference product this was acceptable.

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:

- This product contains benzyl alcohol and may cause skin sensitisation or transient skin reactions in rare cases (for example, irritation, tingling).
- People with known hypersensitivity to imidacloprid should avoid contact with the veterinary medicinal product.
- Avoid contact between the product and skin, eyes or mouth.
- Do not eat, drink or smoke during application.

- Do not massage the application site.
- After application, do not stroke or groom animals until application site is dry.
- Wash off any skin contamination with soap and water.
- Wash hands thoroughly after use.
- If the product gets into eyes accidentally, the eyes should be thoroughly flushed with water.
- If skin or eye irritation persists, obtain medical attention.
- If the product is accidentally swallowed, obtain medical attention immediately.

Environmental Safety

Phase I:
A phase I ERA, written and conducted in accordance with the VICH guideline CVMP/VICH/592/98-Final was submitted.
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

As these applications are generic applications according to Article 3(1) of Directive 2001/82/EC and bioequivalence with a reference product has been established, efficacy studies were not required. The efficacy claims for these products are equivalent to those of the reference products.

IV.I. Pre-Clinical Studies

Pharmacology

Pharmacodynamics and Pharmacokinetics
In accordance with Article 13(1) of Directive 2001/82/EC as amended, no data were submitted.

Tolerance in the Target Species

In accordance with Article 13(1) of Directive 2001/82/EC as amended, no data were submitted.
Warnings in the SPC reflect those of the reference products.

Resistance

In accordance with Article 13(1) of Directive 2001/82/EC as amended, no data were submitted.

IV.II. Clinical Documentation

In accordance with Article 13(1) of Directive 2001/82/EC as amended, no data were submitted.

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 these 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 Heads of Veterinary Medicines Agencies website (www.HMA.eu).
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.

Significant changes

Summary of change (Application number)	**Approval date**
Change of RMS from UK to AT	21/08/2018
No further significant changes until today.	03/08/2021