ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Frontline Combo 268.00 mg / 241.20 mg spot-on solution for dog L
Frontline Comp 268.00 mg / 241.20 mg spot-on solution for dog L [FI SE NO]
Frontline Combo Vet 268.00 mg / 241.20 mg spot-on solution for dog L [DK]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pipette of 2.68 ml contains:

Active substances:

Fipronil ..... 268.00 mg
(S)-methoprene ..... 241.20 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Butylhydroxyanisole (E320)	*0.54 mg*
Butylhydroxytoluene (E321)	*0.27 mg*
Ethanol	
Polysorbate 80 (E433)	
Polyvidone	
Diethylene glycol monoethyl ether	

Clear amber spot-on solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs (weighing 20 to 40 kg bw).

3.2 Indications for use for each target species

To be used against infestations with fleas, alone or in association with ticks and/or biting lice.
- Treatment of flea infestations (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 8 weeks. Prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity) and larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas for eight weeks after application.
- Treatment of tick infestations (*Ixodes ricinus, Dermacentor variabilis, Dermacentor reticulatus, Rhipicephalus sanguineus*). The veterinary medicinal product has a persistent acaricidal efficacy for up to 4 weeks against ticks.
- Treatment of infestations with biting lice (*Trichodectes canis*).

The veterinary medicinal product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).

3.3 Contraindications

In the absence of available data, the veterinary medicinal product should not be used on puppies less than 8 weeks old.
Do not use in rabbits, as adverse reactions with even mortality could occur. In absence of studies, the use of the veterinary medicinal product is not recommended in non-target species.
Do not use on sick (e.g. systemic diseases, fever) or convalescent animals.
This veterinary medicinal product is specifically developed for dogs. Do not use in cats and ferrets, as this could lead to overdosing.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

3.4 Special warnings

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of based on its epidemiological features, for each individual animal.
Bathing/immersion in water within 2 days after application of the veterinary medicinal product and more frequent bathing than once a week should be avoided, as no study has been performed to investigate how this affects the efficacy of the veterinary medicinal product. Emollient shampoos can be used prior to treatment, but reduce the duration of protection against fleas to approximately 5 weeks when used weekly after application of the veterinary medicinal product. Weekly bathing with a 2% chlorhexidine medicated shampoo did not affect efficacy against fleas during a 6 week long study.
There may be an attachment of a few ticks. For this reason a transmission of infectious diseases cannot be completely excluded if conditions are unfavourable.
Fleas from pets often infest the animal's basket, bedding and regular resting areas such as carpets and soft furnishings which should be treated, in case of massive infestation and at the beginning of the control measures, with a suitable insecticide and vacuumed regularly.
Other animals living in the same household should also be treated with a suitable product.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Avoid contact with the animal's eyes.
It is important to make sure that the veterinary medicinal product is applied to an area where the animal cannot lick it off and to make sure that animals do not lick each other following treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

This veterinary medicinal product can cause mucous membrane, skin and eye irritation. Therefore, contact of the veterinary medicinal product with mouth, skin and eyes should be avoided.
People with a known hypersensitivity to fipronil or (S)-methoprene, or alcohol should avoid contact with the veterinary medicinal product. Avoid contents coming into contact with the fingers. If this occurs, wash hands with soap and water.
After accidental ocular exposure the eye should be rinsed carefully with pure water.

Wash hands after use.

Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.

Do not smoke, drink or eat during application.

Special precautions for the protection of the environment:

Dogs should not be allowed to swim in watercourses for 2 days after application (see section 5.5).

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reactions (skin discoloration[1], hair loss[1], itching[1], reddening[1]). Generalised itching or hair loss. Hypersalivation[2], vomiting, respiratory signs. Increased sensitivity to stimulation[3], depression[3], other nervous signs[3].

[1] Transient.
[2] If licking occurs, a brief period of hypersalivation may be observed due mainly to the nature of the carrier.
[3] Reversible.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Can be used during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Spot-on use.

The minimum dose is 6.7 mg/kg bw of fipronil and 6 mg/kg bw of (S)-methoprene, corresponding to one pipette of 2.68 ml (L) per dog (weighing over 20 and up to 40 kg). To ensure a correct dosage, body weight should be determined as accurately as possible. Underdosing could result in ineffective use and may favour resistance development.

For infestations with fleas and/or ticks, the need for and frequency of re-treatment(s)should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle. In the absence of safety studies, the minimum treatment interval is 4 weeks.

Method of administration:
Hold the pipette upright. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette. Snap back the tip. Part the coat on the back of the animal at the base of the neck in front of the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze the pipette several times to empty its contents completely and directly onto the skin in one spot.

Temporary changes to the coat (clumped/greasy hair) may be noted at the application site.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Do not overdose.
No adverse events were observed in target animal safety studies in 8-week-old puppies, growing dogs and dogs weighing about 2 kg treated once at five times the recommended dose. The risk of experiencing adverse events (see section 3.6) may however increase when overdosing, so animals should always be treated with the correct pipette size according to bodyweight.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATC vet code: QP53AX65

The veterinary medicinal product is an insecticidal and acaricidal solution for topical use, containing an association of an adulticidal active ingredient, fipronil, in combination with an ovicidal and larvicidal active ingredient, (S)-methoprene.

4.2 Pharmacodynamics

Fipronil is an insecticide and acaricide belonging to the phenylpyrazole family. It acts by interacting with ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA), thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. This results in uncontrolled activity of the central nervous system and death of insects or acarines. Fipronil kills fleas within 24 hours and ticks *(Dermacentor reticulatus, Dermacentor variabilis, Rhipicephalus sanguineus, Ixodes scapularis, Ixodes ricinus, Haemaphysalis longicornis, Haemaphysalis flava, Haemaphysalis campanulata*) and lice within 48 hours post-exposure.

(S)-Methoprene is an insect growth regulator (IGR) of the class of compounds known as juvenile hormone analogues that inhibit the development of immature stages of insects. This compound mimics the action of juvenile hormone and causes impaired development and death of the developing stages of fleas. The on-animal ovicidal activity of (S)-methoprene results from either direct penetration of the eggshell of newly laid eggs or from absorption through the cuticle of the adult fleas. (S)-methoprene is also effective in preventing flea larvae and pupae from developing, which prevents contamination of the environment of treated animals with the immature stages of fleas.

4.3 Pharmacokinetics

Studies of metabolism of fipronil have demonstrated that the major metabolite is the sulfone derivative of fipronil.
(S)-methoprene is extensively degraded into carbon dioxide and acetate that are subsequently incorporated into endogenous materials.

The pharmacokinetic profiles after topical application of fipronil and (S)-methoprene in combination were studied in dogs in comparison to intravenous dosing of fipronil or (S)-methoprene alone. This

established absorption and other pharmacokinetic parameters. The topical application resulted in low systemic absorption of fipronil (11%) with a mean maximum concentration (C_{max}) of approximately 35 ng/ml fipronil and 55 ng/ml of fipronil sulfone in plasma.
Peak fipronil plasma concentrations are slowly attained (mean t_{max} approximately 101 h), and decline slowly (mean terminal half-life approximately 154 h, highest values are observed for males).
Fipronil is extensively metabolised to fipronil sulfone after topical administration.

Plasma concentrations of (S)-methoprene were below the limit of quantitation (20 ng/ml) in dogs after topical application.

Both (S)-methoprene and fipronil, together with its major metabolite, are well-distributed in the hair coat of a dog within one day after application. The concentrations of fipronil, fipronil sulfone and S-methoprene in the hair coat decrease with time and are detectable for at least 60 days after dosing. Parasites are killed through contact rather than systemic exposure.

No pharmacological interaction between fipronil and (S)-methoprene was noted.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

5.3 Special precautions for storage

Do not store above 30°C. Store in the original package.

5.4 Nature and composition of immediate packaging

Nature of primary packaging

A green pipette composed of a heat-formed shell (polyacrylonitrile-methyl acrylate copolymer / polypropylene) and a film (polyacrylonitrile-methyl acrylate copolymer / aluminium / polyethylene terephthalate).
Or
A green pipette composed of a heat-formed shell (polyethylene / ethylene vinyl alcohol / polyethylene / polypropylene / cyclic-olefin-copolymer / polypropylene) and a film (polyethylene / ethylene vinyl alcohol / polyethylene / aluminium / polyethylene terephthalate).

Sales presentation(s) and administrative number(s) of identification

Blister card of 1 x 2.68 ml pipette with a scored tip
Box of 1 blister card of 3 x 2.68 ml pipettes with a scored tip
Box of 1 blister card of 4 x 2.68 ml pipettes with a scored tip
Box of 2 blister cards of 3 x 2.68 ml pipettes with a scored tip

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
The veterinary medicinal product should not enter water courses as fipronil and (S)-methoprene may be dangerous for fish and other aquatic organisms Do not contaminate ponds, waterways or ditches with the veterinary medicinal product or empty containers.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

7. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

8. DATE OF FIRST AUTHORISATION

To be completed nationally.

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{DD/MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

AT, BG, CZ, DE, DK, ES, ET, FI, FR, HR, HU, IT, LT, LV, MT, NL, PL, PT, RO, SI, SK, SV:
Veterinary medicinal product not subject to prescription.

CY, GR, IE, NO, UK(NI):
Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE - <u>COMBINED LABEL AND PACKAGE LEAFLET (v 9.0)</u>

FRONTLINE COMBO SPOT-ON DOG L
Box of 3 pipettes (or 4 pipettes or 6 pipettes)
CASE N°1: *The text below corresponds to the cases where all the information of the package leaflet CAN be conveyed on the outer packaging and container. Consequently, in that case, no separate leaflet is provided in compliance with the current QRD Template.*

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Frontline Combo 268.00 mg / 241.20 mg spot-on solution for dog L
Frontline Comp 268.00 mg / 241.20 mg spot-on solution for dog L [FI SE NO]
Frontline Combo Vet 268.00 mg / 241.20 mg spot-on solution for dog L [DK]

2. COMPOSITION

Each 2.68 ml pipette contains:
Active substances:
Fipronil..... 268.00 mg
(S)-methoprene..... 241.20 mg
Excipients:
Butylhydroxyanisole (E320)..... 0.54 mg
Butylhydroxytoluene (E321)..... 0.27 mg

FIPRONIL 10% w/v (S) METHOPRENE 9% w/v
[Where there is sufficient space, 'w/v' will be added after the percentages of the active substances. Where there is a lack of space, an asterisk will be added next to the percentages with an explanatory note placed close to the Product name.]

Clear amber spot-on solution.

3. PACKAGE SIZE

3 x 2.68 ml
4 x 2.68 ml
6 x 2.68 ml

4. TARGET SPECIES

DOG L 20 – 40 kg

5. INDICATIONS FOR USE

Indications for use

To be used against infestations with fleas, alone or in association with ticks and/or biting lice.
- Treatment of flea infestations (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 8 weeks. Prevention of the multiplication of fleas by

inhibiting the development of eggs (ovicidal activity), larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas for eight weeks after application.
- Treatment of tick infestations (*Ixodes ricinus*, *Dermacentor variabilis*, *Dermacentor reticulatus*, *Rhipicephalus sanguineus*). The product has a persistent acaricidal efficacy for up to 4 weeks against ticks (based on experimental data).
- Treatment of infestations with biting lice (*Trichodectes canis*).

The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).
Fipronil kills fleas within 24 hours and ticks and lice within 48 hours post-exposure.

6. CONTRAINDICATIONS

Contraindications

In the absence of available data, the product should not be used on puppies less than 8 weeks old.
Do not use in rabbits, as adverse drug reactions with even mortality could occur. In absence of studies, the use of the product is not recommended in non-target species.
Do not use on sick (e.g. systemic diseases, fever) or convalescent animals.
This product is specifically developed for dogs. Do not use in cats and ferrets, as this could lead to overdosing.
In the absence of safety studies, the minimum treatment interval is 4 weeks.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

7. SPECIAL WARNINGS

Special warnings

For external use only.
Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of based on its epidemiological features, for each individual animal.
Bathing/immersion in water within 2 days after application of the product and more frequent bathing than once a week should be avoided, as no study has been performed to investigate how this affects the efficacy of the product. Emollient shampoos can be used prior to treatment, but reduce the duration of protection against fleas to approximately 5 weeks when used weekly after application of the product.
Weekly bathing with a 2% chlorhexidine medicated shampoo did not affect efficacy against fleas during a 6 week long study.
There may be an attachment of a few ticks. For this reason a transmission of infectious diseases cannot be completely excluded if conditions are unfavorable.
Fleas from pets often infest the animal's basket, bedding and regular resting areas such as carpets and soft furnishings which should be treated, in case of massive infestation and at the beginning of the control measures, with a suitable insecticide and vacuumed regularly.
Other animals living in the same household should also be treated with a suitable product.

Special precautions for safe use in the target species:
Avoid contact with the animal's eyes.
It is important to make sure that the product is applied to an area where the animal cannot lick it off and to make sure that animals do not lick each other following treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This product can cause mucous membrane, skin and eye irritation. Therefore, contact of the product with mouth, skin and eyes should be avoided.
People with a known hypersensitivity to fipronil or (S)-methoprene, or alcohol should avoid contact with the veterinary medicinal product. Avoid contents coming into contact with the fingers. If this occurs, wash hands with soap and water.
After accidental exposure the eye should be rinsed carefully with pure water.
Wash hands after use.
Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.
Do not smoke, drink or eat during application.

Special precautions for the protection of the environment:
Dogs should not be allowed to swim in watercourses for 2 days after application (See section Special precautions for disposal).

Pregnancy and lactation:
Can be used during pregnancy and lactation.

Overdose:
Do not overdose.
No adverse events were observed in target animal safety studies in 8-week-old puppies, growing dogs and dogs weighing about 2 kg treated once at five times the recommended dose.
The risk of experiencing adverse event may however increase with overdosing (see Adverse Events) so animals should always be treated with the correct pipette size according to bodyweight.

8. ADVERSE EVENTS

Adverse events

Dogs:
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Application site reactions (skin discoloration[1], hair loss[1], itching[1], reddening[1]). Generalised itching or hair loss. Hypersalivation[2], vomiting, respiratory signs. Increased sensitivity to stimulation[3], depression[3], other nervous signs[3].

[1] Transient.
[2] If licking occurs, a brief period of hypersalivation may be observed due mainly to the nature of the carrier.
[3] Reversible.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details on this label, or via your national reporting system: {national system details}.

9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration

Spot-on use.

Dosage
The minimum dose is 6.7 mg/kg bw of fipronil and 6 mg/kg bw of (S)-methoprene, corresponding to one pipette of 2.68 ml (L) per dog (weighing over 20 and up to 40 kg).
To ensure a correct dosage, body weight should be determined as accurately as possible. Underdosing could result in ineffective use and may favour resistance development.
For infestations with fleas and/or ticks, the need for and frequency of re-treatment(s)should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Temporary changes to the coat (clumped/greasy hair) may be noted at the application site.

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

1-Take the pipette out of its packaging
2-Hold the pipette upright. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette. Snap back the tip.
3-Part the coat on the back of the animal at the base of the neck in front of the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze the pipette several times to empty its contents completely and directly onto the skin in one spot.

11. WITHDRAWAL PERIODS

Withdrawal periods: not applicable.

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Do not store above 30°C. Store in the original package.
Keep out of the sight and reach of children.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton after Exp. The expiry date refers to the last day of that month.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

This veterinary medicinal product should not enter water courses as fipronil and (S)-methoprene may be dangerous for fish and other aquatic organisms. Do not contaminate ponds, waterways or ditches with the product or empty containers.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products

AT, BG, CZ, DE, DK, ES, ET, FI, FR, HR, HU, IT, LT, LV, MT, NL, PL, PT, RO, SI, SK, SV:
Veterinary medicinal product not subject to prescription.

CY, GR, IE, NO, UK(NI):
Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

To be completed nationally.

Pack sizes
Blister card of 1 x 2.68 ml pipette
Box of 1 blister card of 3 x 2.68 ml pipettes
Box of 1 blister card of 4 x 2.68 ml pipettes
Box of 2 blister cards of 3 x 2.68 ml pipettes

Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

{MM/YYYY}
Detailed information on this veterinary medicinal product is available in the Union Product Database.

17. CONTACT DETAILS

Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
To be completed nationally.

Manufacturer responsible for batch release:
Boehringer Ingelheim Animal Health France SCS
4 chemin du Calquet
31000 Toulouse, France

Local representatives and contact details to report suspected adverse reactions:
To be completed nationally.

18. OTHER INFORMATION

19. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

21. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

FRONTLINE COMBO SPOT ON DOG L
Box of 3 pipettes (or 4 pipettes or 6 pipettes)
CASE N°2: *The text below corresponds to the cases where all the information of the package leaflet can not be conveyed on the outer packaging and the container* ***(for example for multilingual packaging)****. Consequently a package leaflet is added (see the corresponding template).*

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FRONTLINE COMBO SPOT-ON DOG L
FRONTLINE COMP SPOT-ON DOG L [FI, SE, NO]
FRONTLINE COMBO VET SPOT-ON DOG L [DK]

2. STATEMENT OF ACTIVE SUBSTANCES

Each 2.68 ml pipette contains:
Fipronil..... 268.00 mg
(S)-methoprene..... 241.20 mg

FIPRONIL 10% w/v (S) METHOPRENE 9% w/v
[Where there is sufficient space, 'w/v' will be added after the percentages of the active substances. Where there is a lack of space, an asterisk will be added next to the percentages with an explanatory note placed close to the Product name.]

3. PACKAGE SIZE

3 x 2.68 ml
4 x 2.68 ml
6 x 2.68 ml

4. TARGET SPECIES

DOG L 20 – 40 kg

5. INDICATIONS

For products not subject to veterinary prescription:
Kills fleas on your dog and protects against re-infestation for 8 weeks.

Inhibits the development of flea eggs, flea larvae and pupae for 8 weeks, thus preventing contamination of your dog's environment for the same period.

Kills ticks on your dog and protects against re-infestation for up to 4 weeks.

Kills biting lice.

The duration of protection of FRONTLINE COMBO Spot-On is not affected by immersion in water or weekly shampooing with a 2% Chlorhexidine shampoo for up to 6 weeks when carried out 2 days after treatment.

Can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).

Prevents contamination of the environment of treated animals with the immature stages of fleas.

6. ROUTES OF ADMINISTRATION

Spot-on use.

METHOD OF ADMINISTRATION

1-Take the pipette out of its packaging
2-Hold the pipette upright. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette. Snap back the tip.
3-Part the coat on the back of the animal at the base of the neck in front of the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze the pipette several times to empty its contents completely and directly onto the skin in one spot.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C. Store in the original package.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally.

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

FRONTLINE COMBO SPOT-ON DOG L
Blister card of 1 pipette
The information mentioned below is all the information visible externally on this packaging, either on the blister card or on the combined label package-leaflet inserted in it.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FRONTLINE COMBO SPOT-ON DOG L
FRONTLINE COMP SPOT-ON DOG L [FI, SE, NO]
FRONTLINE COMBO VET SPOT-ON DOG L [DK]

2. STATEMENT OF ACTIVE SUBSTANCES

Each 2.68 ml pipette contains:

Fipronil	268.00 mg
(S)-methoprene	241.20 mg

FIPRONIL 10% w/v (S) METHOPRENE 9% w/v
[Where there is sufficient space, 'w/v' will be added after the percentages of the active substances. Where there is a lack of space, an asterisk will be added next to the percentages with an explanatory note placed close to the Product name.]

3. PACKAGE SIZE

2.68 ml

4. TARGET SPECIES

DOG L 20 – 40 kg

5. INDICATIONS

For Dogs from 8 weeks of age.
For products not subject to veterinary prescription:
Kills fleas
Kills ticks
Kills biting lice
Prevents contamination of the environment of treated animals with the immature stages of fleas.

6. ROUTES OF ADMINISTRATION

Spot-on use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30°C. Store in the original package.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally.

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

FRONTLINE COMBO SPOT ON DOG L
1 pipette
The Immediate packaging is a pipette: the information below appears on the shell or on the opercule of the pipette.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FRONTLINE COMBO L
FRONTLINE COMP L [FI, SE, NO]
FRONTLINE COMBO VET L [DK]

[Pictogram of a drop of product falling from a pipette on the skin of the animal thus showing the route of administration]

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

2.68 ml:
FIPRONIL 268 mg
(S)-METHOPRENE 241.2 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS BLISTERS OR STRIPS

FRONTLINE COMBO SPOT-ON DOG L
Box of 3 pipettes: 1 blister of 3 pipettes
Box of 4 pipettes: 1 blister of 4 pipettes
Box of 6 pipettes: 2 blisters of 3 pipettes
The blister package is the same in both cases: the information below appears on the blister shell or on the blister cap of the blister package.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FRONTLINE COMBO DOG L
FRONTLINE COMP DOG L [FI, SE, NO]
FRONTLINE COMBO VET DOG L [DK]

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

FIPRONIL (S) METHOPRENE
268.0 mg / 241.20 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Box of 3 pipettes
Box of 4 pipettes
Box of 6 pipettes
The leaflet described below applies to Case N°2 where a package leaflet is added in the packaging.
In case N°1 no leaflet is added.

1. Name of the veterinary medicinal product

Frontline Combo 268.00 mg / 241.20 mg spot-on solution for dog L
Frontline Comp 268.00 mg / 241.20 mg spot-on solution for dog L [FI SE NO]
Frontline Combo Vet 268.00 mg / 241.20 mg spot-on solution for dog L [DK]

2. Composition

Each 2.68 ml pipette contains:

Active substances:
Fipronil ..... 268.00 mg
(S)-methoprene ..... 241.20 mg

Excipients:
Butylhydroxyanisole (E320) ..... 0.54 mg
Butylhydroxytoluene (E321) ..... 0.27 mg

Clear amber spot-on solution.

3. Target species

Dogs (weighing 20 to 40 kg bw).

4. Indications for use

To be used against infestations with fleas, alone or in association with ticks and/or biting lice.
- Treatment of flea infestations (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 8 weeks. Prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity), larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas for eight weeks after application.
- Treatment of tick infestations (*Ixodes ricinus*, *Dermacentor variabilis*, *Dermacentor reticulatus*, *Rhipicephalus sanguineus*). The product has a persistent acaricidal efficacy for up to 4 weeks against ticks (based on experimental data).
- Treatment of infestations with biting lice (*Trichodectes canis*).

The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).

5. Contraindications

In the absence of available data, the product should not be used on puppies less than 8 weeks old.
Do not use in rabbits, as adverse drug reactions with even mortality could occur. In absence of studies, the use of the product is not recommended in non-target species.

Do not use on sick (e.g. systemic diseases, fever) or convalescent animals.
This product is specifically developed for dogs. Do not use in cats and ferrets, as this could lead to overdosing.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

6. Special warnings

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of based on its epidemiological features, for each individual animal.
Bathing/immersion in water within 2 days after application of the product and more frequent bathing than once a week should be avoided, as no study has been performed to investigate how this affects the efficacy of the product. Emollient shampoos can be used prior to treatment, but reduce the duration of protection against fleas to approximately 5 weeks when used weekly after application of the product. Weekly bathing with a 2% chlorhexidine medicated shampoo did not affect efficacy against fleas during a 6 week long study.

There may be an attachment of a few ticks. For this reason a transmission of infectious diseases cannot be completely excluded if conditions are unfavourable.
Fleas from pets often infest the animal's basket, bedding and regular resting areas such as carpets and soft furnishings which should be treated, in case of massive infestation and at the beginning of the control measures, with a suitable insecticide and vacuumed regularly.
Other animals living in the same household should also be treated with a suitable product.

Special precautions for safe use in the target species:

Avoid the contact with the animal’s eyes.
It is important to make sure that the product is applied to an area where the animal cannot lick it off and to make sure that animals do not lick each other following treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

This product can cause mucous membrane, skin and eye irritation. Therefore, contact of the product with mouth, skin and eyes should be avoided.
People with a known hypersensitivity to fipronil or (S)-methoprene, or alcohol should avoid contact with the veterinary medicinal product. Avoid contents coming into contact with the fingers. If this occurs, wash hands with soap and water.
After accidental exposure the eye should be rinsed carefully with pure water.
Wash hands after use.
Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.

Do not smoke, drink or eat during application.

Special precautions for the protection of the environment:

Dogs should not be allowed to swim in watercourses for 2 days after application (see section Special precautions for disposal).

Pregnancy and lactation:

Can be used during pregnancy and lactation.

Overdose:

Do not overdose.
No adverse events were observed in target animal safety studies in 8-week-old puppies, growing dogs and dogs weighing about 2 kg treated once at five times the recommended dose.
The risk of experiencing adverse event may however increase with overdosing (see Adverse Events) so animals should always be treated with the correct pipette size according to bodyweight.

7. Adverse events

Dogs:
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Application site reactions (skin discoloration[1], hair loss[1], itching[1], reddening[1]). Generalised itching or hair loss. Hypersalivation[2], vomiting, respiratory signs. Increased sensitivity to stimulation[3], depression[3], other nervous signs[3].

[1] Transient.
[2] If licking occurs, a brief period of hypersalivation may be observed due mainly to the nature of the carrier.
[3] Reversible.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

Spot-on use.

The minimum dose is 6.7 mg/kg bw of fipronil and 6 mg/kg bw of (S)-methoprene, corresponding to one pipette of 2.68 ml (L) per dog (weighing over 20 and up to 40 kg). To ensure a correct dosage, body weight should be determined as accurately as possible. Underdosing could result in ineffective use and may favour resistance development.

For infestations with fleas and/or ticks, the need for and frequency of re-treatment(s)should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle. In the absence of safety studies, the minimum treatment interval is 4 weeks.
Temporary changes to the coat (clumped/greasy hair) may be noted at the application site.

9. Advice on correct administration

Method of administration: see outer packaging.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 30 °C. Store in the original package.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

This veterinary medicinal product should not enter water courses as fipronil and (S)-methoprene may be dangerous for fish and other aquatic organisms. Do not contaminate ponds, waterways or ditches with the product or empty containers.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

AT, BG, CZ, DE, DK, ES, ET, FI, FR, HR, HU, IT, LT, LV, MT, NL, PL, PT, RO, SI, SK, SV:
Veterinary medicinal product not subject to prescription.

CY, GR, IE, NO, UK(NI):
Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

To be completed nationally.

Blister card of 1 x 2.68 ml pipette
Box of 1 blister card of 3 x 2.68 ml pipettes
Box of 1 blister card of 4 x 2.68 ml pipettes
Box of 2 blister cards of 3 x 2.68 ml pipettes

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}
Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
To be completed nationally.

Manufacturer responsible for batch release:
Boehringer Ingelheim Animal Health France SCS
4 chemin du Calquet
31000 Toulouse
France

Local representatives and contact details to report suspected adverse reactions:
To be completed nationally.

17. Other information

Pharmacodynamics:
Fipronil kills fleas within 24 hours and ticks and lice within 48 hours post-exposure.

FRONTLINE COMBO SPOT-ON DOG L
FRONTLINE COMP SPOT-ON DOG L [FI, SE, NO]
FRONTLINE COMBO VET SPOT-ON DOG L [DK]

Combined label and package leaflet for Blister card of 1 pipette
The information mentioned below appears on the interior side of this combined label package-leaflet.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Frontline Combo 268.00 mg / 241.20 mg spot-on solution for dog L
Frontline Comp 268.00 mg / 241.20 mg spot-on solution for dog L [FI SE NO]
Frontline Combo Vet 268.00 mg / 241.20 mg spot-on solution for dog L [DK]

2. COMPOSITION

Each 2.68 ml pipette contains:
Active substances:
Fipronil..... 268.00 mg
(S)-methoprene..... 241.20 mg
Excipients:
Butylhydroxyanisole (E320) ..... 0.54 mg
Butylhydroxytoluene (E321)..... 0.27 mg

FIPRONIL 10% w/v (S) METHOPRENE 9% w/v
[Where there is sufficient space, 'w/v' will be added after the percentages of the active substances. Where there is a lack of space, an asterisk will be added next to the percentages with an explanatory note placed close to the Product name.]

Clear amber spot-on solution

3. PACKAGE SIZE

2.68 ml

4. TARGET SPECIES

DOG L 20 – 40 kg

5. INDICATIONS FOR USE

Indications for use

To be used against infestations with fleas, alone or in association with ticks and/or biting lice.
- Treatment of flea infestations (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 8 weeks. Prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity), larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas for eight weeks after application.
- Treatment of tick infestations (*Ixodes ricinus*, *Dermacentor variabilis*, *Dermacentor reticulatus*, *Rhipicephalus sanguineus*). The product has a persistent acaricidal efficacy for up to 4 weeks against ticks (based on experimental data).

- Treatment of infestations with biting lice (*Trichodectes canis*).

The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).

6. CONTRAINDICATIONS

Contraindications

In the absence of available data, the product should not be used on puppies less than 8 weeks old.
Do not use in rabbits, as adverse drug reactions with even mortality could occur. In absence of studies, the use of the product is not recommended in non-target species.
Do not use on sick (e.g. systemic diseases, fever) or convalescent animals.
This product is specifically developed for dogs. Do not use in cats and ferrets, as this could lead to overdosing.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

7. SPECIAL WARNINGS

Special warnings

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of based on its epidemiological features, for each individual animal.
Bathing/immersion in water within 2 days after application of the product and more frequent bathing than once a week should be avoided, as no study has been performed to investigate how this affects the efficacy of the product. Emollient shampoos can be used prior to treatment, but reduce the duration of protection against fleas to approximately 5 weeks when used weekly after application of the product. Weekly bathing with a 2% chlorhexidine medicated shampoo did not affect efficacy against fleas during a 6 week long study.
There may be an attachment of a few ticks. For this reason a transmission of infectious diseases cannot be completely excluded if conditions are unfavourable.
Fleas from pets often infest the animal's basket, bedding and regular resting areas such as carpets and soft furnishings which should be treated, in case of massive infestation and at the beginning of the control measures, with a suitable insecticide and vacuumed regularly.
Other animals living in the same household should also be treated with a suitable product.

Special precautions for safe use in the target species:

Avoid the contact with the animal’s eyes.
It is important to make sure that the product is applied to an area where the animal cannot lick it off and to make sure that animals do not lick each other following treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

This product can cause mucous membrane, skin and eye irritation. Therefore, contact of the product with mouth, skin and eyes should be avoided.
People with a known hypersensitivity to fipronil or (S)-methoprene, or alcohol should avoid contact with the veterinary medicinal product. Avoid contents coming into contact with the fingers. If this occurs, wash hands with soap and water.
After accidental exposure the eye should be rinsed carefully with pure water.
Wash hands after use.

Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.
Do not smoke, drink or eat during application.

Special precautions for the protection of the environment:

Dogs should not be allowed to swim in watercourses for 2 days after application (see section Special precautions for disposal).

Pregnancy and lactation:

Can be used during pregnancy and lactation.

Overdose:

Do not overdose.

No adverse events were observed in target animal safety studies in 8-week-old puppies, growing dogs and dogs weighing about 2 kg treated once at five times the recommended dose.
The risk of experiencing adverse event may however increase with overdosing (see Adverse Events) so animals should always be treated with the correct pipette size according to bodyweight.

8. ADVERSE EVENTS

Adverse events

Dogs:
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Application site reactions (skin discoloration[1], hair loss[1], itching[1], reddening[1]). Generalised itching or hair loss. Hypersalivation[2], vomiting, respiratory signs. Increased sensitivity to stimulation[3], depression[3], other nervous signs[3].

[1] Transient.
[2] If licking occurs, a brief period of hypersalivation may be observed due mainly to the nature of the carrier.
[3] Reversible.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details on this label, or via your national reporting system: {national system details}.

9. DOSAGE FOR EACH SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration

Spot-on use.
The minimum dose is 6.7 mg/kg bw of fipronil and 6 mg/kg bw of (S)-methoprene, corresponding to one pipette of 2.68 ml (L) per dog (weighing over 20 and up to 40 kg).

To ensure a correct dosage, body weight should be determined as accurately as possible. Underdosing could result in ineffective use and may favour resistance development.

For infestations with fleas and/or ticks, the need for and frequency of re-treatment(s)should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle. In the absence of safety studies, the minimum treatment interval is 4 weeks.

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

1-Tak**e** the pipette out of its packaging.
2-Hold the pipette upright. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette. Snap back the tip.
3-Part the coat on the back of the animal at the base of the neck in front of the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze the pipette several times to empty its contents completely and directly onto the skin in one spot.
Temporary changes to the coat (clumped/greasy hair) may be noted at the application site.

11. WITHDRAWAL PERIODS

Withdrawal periods: not applicable.

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Do not store above 30 °C. Store in the original package.
Keep out of the sight and reach of children.
Do not use this veterinary medicinal product after the expiry date which is stated on the blister card after Exp. The expiry date refers to the last day of that month.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

This veterinary medicinal product should not enter water courses as fipronil and (S)-methoprene may be dangerous for fish and other aquatic organisms. Do not contaminate ponds, waterways or ditches with the product or empty containers.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products

AT, BG, CZ, DE, DK, ES, ET, FI, FR, HR, HU, IT, LT, LV, MT, NL, PL, PT, RO, SI, SK, SV:
Veterinary medicinal product not subject to prescription.

CY, GR, IE, NO, UK(NI):
Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

To be completed nationally.

Pack sizes
Blister card of 1 x 2.68 ml pipette
Box of 1 blister card of 3 x 2.68 ml pipettes
Box of 1 blister card of 4 x 2.68 ml pipettes
Box of 2 blister cards of 3 x 2.68 ml pipettes

Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

{MM/YYYY}
Detailed information on this veterinary medicinal product is available in the Union Product Database.

17. CONTACT DETAILS

Marketing authorisation holder and contact details to report suspected adverse reactions:
To be completed nationally.

Manufacturer responsible for batch release:
Boehringer Ingelheim Animal Health France SCS
4 chemin du Calquet
31000 Toulouse
France

Local representatives and contact details to report suspected adverse reactions:
To be completed nationally.

18. OTHER INFORMATION

Other information

Pharmacodynamics:
Fipronil kills fleas within 24 hours and ticks and lice within 48 hours post-exposure.

19. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

21. BATCH NUMBER

Lot {number}