1. NAME OF THE VETERINARY MEDICINAL PRODUCT

IE, LT, RO, BG, EL, HU, IT, PL	**FIPREX DUO XL** 402 mg + 361.8 mg spot-on solution for dogs
PT	**FIPON DUO XL** 402 mg + 361.8 mg spot-on solution for dogs
ES	**FIPREX DUO** 402 mg + 361.8 mg spot-on solution for extra large dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pipette of 4.02 ml contains:

Active substances:

Fipronil 402.00 mg
(S)-methoprene 361.80 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)	0.80 mg
Butylhydroxytoluene (E321)	0.40 mg
Ethanol (96 per cent)	
Polysorbate 80	
Povidone K17	
Diethylene glycol monoethyl ether	

Clear greenish-yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs (>40 kg).

3.2 Indications for use for each target species

For the treatment of dogs weighing over 40 kg bodyweight.

- 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 persist 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), where this has been previously diagnosed by a veterinary surgeon.

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 on sick (e.g. systemic diseases, fever) or convalescent animals.
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.
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

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 veterinary medicinal product.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Avoid contact with the animal’s eyes.
Do not apply the veterinary medicinal product on wounds or damaged skin.
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 known hypersensitivity to insecticides 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.

Ingestion of the veterinary medicinal product may be harmful. Prevent children getting access to the pipettes and discard the used pipettes immediately after applying the veterinary medicinal product. In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

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.

The alcohol carrier may have adverse effects on painted, varnished or other household surfaces or furnishings.

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[1] (application site skin discolouration, localised hair loss, application site itching, reddening of the skin); General hair loss, Generalised itching; Hypersalivation[2], Vomiting; Nervous signs[3] (increased sensitivity to stimulation, depression, other nervous signs); Respiratory signs.

[1] Transient.
[2] If licking occurs, a brief period of excessive salivation 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

Pregnancy and lactation:

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.

Dosage:

One pipette of 4.02 ml per dog weighing over 40 kg, corresponding to a minimum recommended dose of 6.7 mg/kg for fipronil and 6 mg/kg for (S)-methoprene, by topical application to the skin.
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)

No adverse effects 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 ATCvet code: QP53AX65

4.2 Pharmacodynamics

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.
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 hours), and decline slowly (mean terminal half-life approximately 154 hours, 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 haircoat 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

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 20 months

5.3 Special precautions for storage

Store in the original package in order to protect from light and moisture. Store below 25 °C.

5.4 Nature and composition of immediate packaging

A red pipette composed of a heat-formed shell (internal layer PE/EVOH/PE external layer PP/COC/PP) and a film (PET/PE/ALU/PE).

Package size:

1 x 4.02 ml pipette in carton box.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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.

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

Vet-Agro Multi-Trade Company Sp. z o.o.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription. (IE, EL)
Veterinary medicinal product not subject to prescription. (ES, HU, RO, PT, IT, PL, LT, BG)

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

Carton box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FIPREX DUO XL 402 mg + 361.8 mg spot-on solution

2. STATEMENT OF ACTIVE SUBSTANCES

Each pipette of 4.02 ml contains:

Active substances:
Fipronil 402.00 mg
(S)-methoprene 361.80 mg

3. PACKAGE SIZE

4.02 ml

4. TARGET SPECIES

Dogs (>40 kg)

5. INDICATIONS

For products not subject to veterinary prescription

For the treatment of dogs weighing over 40 kg bodyweight

- 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 persist 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), where this has been previously diagnosed by a veterinary surgeon.

[Two pictograms - one showing a tick inside a crossed-out circle and the other showing a flea inside a crossed-out circle]

6. ROUTES OF ADMINISTRATION

Spot on use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store in the original package in order to protect from light and moisture. Store below 25 °C.

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

{Logo name of the marketing authorisation holder}

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

[Three pictograms:
1- pictogram showing a broached pipette and two arrows - correct place to break the pipette
2- pictogram showing a standing dog and the pipette above the neck - the correct place to administer the product
3- pictogram showing a hand parting the fur and the pipette above this place - the correct way to administer the product]



MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PIPETTE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FIPREX DUO XL

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

4.02 ml:

Fipronil	402.00 mg
(S)-methoprene	361.80 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Spot-on use

{Logo name of the marketing authorisation holder}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

FIPREX DUO XL 402 mg + 361.8 mg spot-on solution for dogs

2. Composition

Each pipette of 4.02 ml contains:

Active substances:
Fipronil 402.00 mg
(S)-methoprene 361.80 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)	0.80 mg
Butylhydroxytoluene (E321)	0.40 mg

Clear greenish-yellow solution.

3. Target species

Dogs (>40 kg).

4. Indications for use

For the treatment of dogs weighing over 40 kg bodyweight.

- 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 persist 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), where this has been previously diagnosed by a veterinary surgeon.

5. 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 on sick (e.g. systemic diseases, fever) or convalescent animals.
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.

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.

6. Special warnings

Special warnings:

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 veterinary medicinal product.

Special precautions for safe use in the target species:

Avoid contact with the animal’s eyes.
Do not apply the veterinary medicinal product on wounds or damaged skin.

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 known hypersensitivity to insecticides 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.

Ingestion of the veterinary medicinal product may be harmful. Prevent children getting access to the pipettes and discard the used pipettes immediately after applying the veterinary medicinal product. In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

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.

The alcohol carrier may have adverse effects on painted, varnished or other household surfaces or furnishings.

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.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose:
No adverse effects 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 "Adverse events") may however increase when overdosing, 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[1] (application site skin discolouration, localised hair loss, application site itching, reddening of the skin); General hair loss, Generalised itching; Hypersalivation[2], Vomiting; Nervous signs[3] (increased sensitivity to stimulation, depression, other nervous signs); Respiratory signs.

[1] Transient.
[2] If licking occurs, a brief period of excessive salivation 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.

One pipette of 4.02 ml per dog weighing over 40 kg, corresponding to a minimum recommended dose of 6.7 mg/kg for fipronil and 6 mg/kg for (S)-methoprene, by topical application to the skin.
In the absence of safety studies, the minimum treatment interval is 4 weeks.

9. Advice on correct 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.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store in the original package in order to protect from light and moisture. Store below 25 °C.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and pipette after Exp.

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.

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

Veterinary medicinal product subject to prescription. (IE, EL)
Veterinary medicinal product not subject to prescription. (ES, HU, RO, PT, IT, PL, LT, BG)

14. Marketing authorisation numbers and pack sizes

Package size:
1 x 4.02 ml pipette in carton box.

15. Date on which the package leaflet was last revised

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:
Vet-Agro Multi-Trade Company Sp. z o.o.
Gliniana 32, 20-616 Lublin, Poland

Manufacturer responsible for batch release:
Vet-Agro Multi Trade Company Sp. z o.o.
Mełgiewska 18, 20-234 Lublin, Poland

Local representatives <and contact details to report suspected adverse reactions>:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information