

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zeronil Combo 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs. (IE)
Purviso Flea 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs. (FR, NL)
Fipnil Combo 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs. (BG, EL, IT, RO, CZ, HU, PL, SK)
Fiprosmet 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs. (ES, PT)

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, anhydrous	
Polysorbate 80	
Povidone K17	
Diethylene glycol monoethyl ether	

Clear amber solution.

3. CLINICAL PARTICULARS

3.1 Target Species

Dogs.

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 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).

3.3 Contraindications

In the absence of available data, the veterinary medicinal product should not be used on puppies less than 8 weeks old and/or weighing less than 2 kg.

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.

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 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.

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:

See section 5.5.

Other precautions:

Not applicable.

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reactions (Skin discoloration, Hair loss, Itching, Reddening of skin) ¹ . Generalised itching, Hair loss. Hypersalivation ³ , Vomiting. Increased sensitivity to stimulation ² , Depression ² , Other nervous signs ² . Respiratory signs.
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¹Transient.

² Reversible.

³If licking occurs, a brief period of excessive salivation may be observed due mainly to the nature of the carrier.

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.

One pipette of 4.02 ml (XL) 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:

1. Hold the pipette upright.

2. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette.
3. Snap back the tip.
4. 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.
5. 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 effects (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 Period(s)

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP53AX65

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 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

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 36 months.

5.3 Special precautions for storage

Store in the original package in order to protect from light.

5.4 Nature and composition of immediate packaging

A white pipette composed of a heat-formed shell of polypropylene/cyclic olefin copolymer/polypropylene layer and polyethylene/ethylene vinyl alcohol/polyethylene layer.

Box with 1, 2, 3, 4, 6, 8, 9, 10, 12, 15, 18, 20, 21, 24, 30, 60, 90, 150 or 160 pipettes in individual foil sachets.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

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.

The veterinary medicinal product should not enter water courses as fipronil and (S)-methoprene may be dangerous for fish and other aquatic organisms.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd,

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF THE FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription (IE, EL)

Veterinary medicinal product not subject to prescription (RO, IT, SK, BG, HU, FR, ES, PT, PL)

Veterinary medicinal product subject to veterinary prescription except for some pack sizes (CZ)

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}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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Fipnil Combo 402 mg/361.8 mg Spot-on Solution. (BG, EL, IT, RO, CZ, HU, PL, SK)
Fiprosmet 402 mg/361.8 mg Spot-on Solution. (ES, PT)

2. STATEMENT OF ACTIVE SUBSTANCES

Each pipette: Fipronil 402.00 mg, (S)-methoprene 361.80 mg.

3. PACKAGE SIZE

1 x 4.02 ml
2 x 4.02 ml
3 x 4.02 ml
4 x 4.02 ml
6 x 4.02 ml
8 x 4.02 ml
9 x 4.02 ml
10 x 4.02 ml
12 x 4.02 ml
15 x 4.02 ml
18 x 4.02 ml
20 x 4.02 ml
21 x 4.02 ml
24 x 4.02 ml
30 x 4.02 ml
60 x 4.02 ml
90 x 4.02 ml
150 x 4.02 ml
160 x 4.02 ml

4. TARGET SPECIES

Dogs

5. INDICATIONS

For products not subject to veterinary prescription
Treats fleas, ticks and biting lice.

6. ROUTES OF ADMINISTRATION

Spot-on

7. WITHDRAWAL PERIOD

8. EXPIRY DATE

Exp {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store in the original package in order to protect from light.

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





Chanelle Pharmaceuticals Manufacturing Ltd,

14. MARKETING AUTHORISATION NUMBER(S)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**{Pipette}****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Zeronil Combo  (IE)
Purviso Flea  (FR, NL)
Fipnil Combo  (BG, EL, IT, RO, CZ, HU, PL, SK)
Fiprosmet  (ES, PT)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE(S)

4.02 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp {mm/yyyy}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**{Sachet}****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Zeronil Combo Spot-on Solution for Extra Large Dogs. (IE)

Purviso Flea Spot-on Solution for Extra Large Dogs. (FR, NL)

Fipnil Combo Spot-on Solution for Extra Large Dogs. (BG, EL, IT, RO, CZ, HU, PL, SK)

Fiprosmet Spot-on Solution for Extra Large Dogs. (ES, PT)

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Fipronil 402 mg (S)-methoprene 361.8 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zeronil Combo 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs. (IE)
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Fipnil Combo 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs. (BG, EL, IT, RO, CZ, HU, PL, SK)
Fiprosmet 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs. (ES, PT)

2. COMPOSITION

Each pipette of 4.02 ml contains:

Active substances:

Fipronil	402.00 mg
(S)-methoprene	361.80 mg

Excipients:

Butylhydroxyanisole (E320)	0.80 mg
Butylhydroxytoluene (E321)	0.40 mg

Clear amber solution.

3. TARGET SPECIES

Dogs.

4. INDICATION(S) FOR USE

- To be used against infestations with fleas, alone or in association with ticks and/or biting lice.
- Treatment of flea infestations (of the species *Ctenocephalides* spp.). Prevention of new infestations with adult fleas persists for 8 weeks. Prevention of the multiplication of fleas by stopping the development of eggs, and larvae and pupae originating from eggs laid by adult fleas for eight weeks after application.
- Treatment of tick infestations (of the species *Ixodes ricinus*, *Dermacentor variabilis*, *Dermacentor reticulatus*, *Rhipicephalus sanguineus*) for up to 4 weeks.
- Treatment of infestations with biting lice (of the species *Trichodectes canis*).

5. CONTRAINDICATIONS

The veterinary medicinal product should not be used on puppies less than 8 weeks old and/or weighing less than 2 kg.

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.

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 WARNING(S)

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.

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 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.

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:

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 (symptoms, emergency procedures, 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 effects may however increase when overdosing, so animals should always be treated with the correct pipette size according to bodyweight.

7. ADVERSE REACTIONS

Dogs

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reactions (Skin discoloration, Hair loss, Itching, Reddening of skin) ¹ . Generalised itching, Hair loss. Hypersalivation ³ , Vomiting. Increased sensitivity to stimulation ² , Depression ² , Other nervous signs ² . Respiratory signs
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¹Transient.

² Reversible.

³If licking occurs, a brief period of excessive salivation may be observed due mainly to the nature of the carrier.

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.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Spot-on use.

Administer by topical application to the skin according to the bodyweight as follows.

The minimum treatment interval is 4 weeks.

Bodyweight	Dose
Over 40 kg	1 pipette of Zeronil Combo/ Purviso Flea /Fipnil Combo/Fiprosmet 402 mg/361.8 mg Spot-on Solution for Extra Large Dogs

Method of administration:

1. Hold the pipette upright.
2. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette.
3. Snap back the tip.

4. 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.
5. 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.

9. ADVICE ON CORRECT ADMINISTRATION

Discard any opened pipettes.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

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 and label after {Exp.}. The expiry date refers to the last day of that month.

Store in the original package in order to protect from light.

12. SPECIAL PRECAUTIONS FOR DISPOSAL

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

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.

The veterinary medicinal product should not enter water courses as Fipronil and (S)-methoprene may be dangerous for fish and other aquatic organisms.

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 (RO, IT, SK, BG, HU, CZ, FR, ES, PT, PL)

Veterinary medicinal product subject to veterinary prescription except for some pack sizes (CZ)

14. Marketing authorisation numbers and pack sizes

Box with 1, 2, 3, 4, 6, 8, 9, 10, 12, 15, 18, 20, 21, 24, 30, 60, 90, 150 or 160 pipettes in individual foil sachets.

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 manufacturer responsible for batch release and contact details to report suspected adverse reactions:

Chanelle Pharmaceuticals Manufacturing Ltd.,
Loughrea,
Co. Galway.
Ireland.
Telephone: +353 (0)91 841788
vetpharmacoviggroup@chanellegroup.ie

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

