

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Amflee Combo 50 mg/60 mg spot-on solution for cats (CY, IE)

Fyperix Combo 50 mg/60 mg spot-on solution for cats (PT)

Fyperix Comp vet 50 mg/60 mg spot-on solution for cats (FI)

Fypermid Combo 50 mg/60 mg spot-on solution for cats (IT)

Fleascreen Combo 50 mg/60 mg spot-on solution for cats (BE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 ml pipette contains:

Active substances:

Fipronil 50 mg

S-Methoprene 60 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)	0.1 mg
Butylhydroxytoluene (E321)	0.05 mg
Povidone (K25)	
Polysorbate 80	
Ethanol 96 per cent	
Diethylene glycol monoethyl ether	

Clear yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Cats.

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 fleas (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 4 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 six weeks after application.
- Treatment of ticks (*Ixodes ricinus*, *Dermacentor variabilis*, *Rhipicephalus sanguineus*). The veterinary medicinal product has a persistent acaricidal efficacy for up to 2 weeks against ticks (based on experimental data).
- Treatment of biting lice (*Felicola subrostratus*).

3.3 Contraindications

Do not use on kittens less than 8 weeks old and/or weighing less than 1 kg.
Do not use on sick (e.g. systemic diseases, fever) or convalescent animals.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Do not use in rabbits, as adverse drug reactions with even mortality could occur.
Do not use in any other non-target species.

3.4 Special warnings

When treating infestations of parasites, all in-contact animals should be treated with an appropriate veterinary medicinal product at the same time. 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.

Bathing and/or shampooing should be avoided. No information on the effect of bathing or the use of a shampoo on the effectiveness of the veterinary medicinal product in cats is available. Based on information available for dogs, 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.

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.

There may be an attachment of single ticks. For this reason a transmission of infectious diseases cannot be completely excluded if conditions are unfavourable.

The potential toxicity of the veterinary medicinal product for kittens of less than 8 weeks of age in contact with a treated queen is not documented. Special care should be taken in this case.

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 (allergy) 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 in clean water.

In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

Do not smoke, drink or eat during application.

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.

Keep pipettes in original packaging until ready to use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cats:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reactions (skin scaling, localised hair loss, itching, reddening) ¹ Skin and appendages disorders (itching, hair loss)
Undetermined frequency (cannot be estimated from the available data):	Digestive tract disorders (hypersalivation, vomiting) Neurological disorders (increased sensitivity to stimulation, depression, other nervous signs) ²

¹Transient.

²Reversible.

In the case of licking the administration site, 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.
See section 3.5.

3.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with other flea products which are applied directly on to the animal.

3.9 Administration routes and dosage

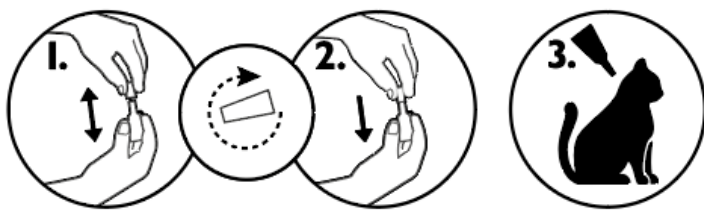
Spot-on use.

One pipette of 0.5 ml per cat, corresponding to a minimum recommended dose of 5 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. Remove the pipette from its packaging. Hold the pipette in an upright position, twist and pull the cap off.
2. Turn the cap around and place the other end of the cap back on the pipette. Push and twist the cap to break the seal, then remove the cap from the pipette.
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 onto the skin and squeeze the pipette several times to empty its contents completely and directly onto the skin in one spot.



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

The risk of experiencing adverse effects may increase with overdosing (see section 3.6).

No undesirable effects were observed in target animal safety studies in cats and kittens aged 8 weeks and older and weighing about 1 kg treated once a month at five times the recommended dose for six consecutive months.

Itching may occur following treatment.

Overdose application of the veterinary medicinal product will cause a sticky appearance of hairs at the treatment spot. However, should this occur, it will disappear within 24 hours post application.

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

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, ticks (*Dermacentor variabilis*, *Rhipicephalus sanguineus* and *Ixodes ricinus*) 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 cats in comparison to intravenous dosing of fipronil or (S)-methoprene alone. This established absorption and other pharmacokinetic parameters under conditions mimicking clinical practice. The topical application, with additional potential oral exposure from licking, resulted in overall systemic absorption of fipronil (18 %) with a mean maximum concentration (C_{\max}) of approximately 100 ng/ml fipronil and 13 ng/ml of fipronil sulfone in plasma. Peak fipronil plasma concentrations are rapidly attained (mean t_{\max} approximately 6 hours) and decline with a mean terminal half-life of approximately 25 hours. Fipronil is slightly metabolised to fipronil sulfone in cats.

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

Both (S)-methoprene and fipronil, together with its major metabolite, are well-distributed in the haircoat of cats 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 59 days after dosing. Parasites are killed through contact rather than by 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: 2 years.

5.3 Special precautions for storage

Store below 30 °C.

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

5.4 Nature and composition of immediate packaging

White polypropylene single-dose pipette packaged in aluminium foil sachets.

Pack sizes:

Cardboard box containing 1, 3, 6 or 30 pipettes.

Not all pack sizes may be marketed.

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

KRKA, d.d., Novo mesto

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: <{DD/MM/YYYY}><{DD month YYYY}>.

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

<{MM/YYYY}>

<{DD/MM/YYYY}>

<{DD month YYYY}>

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product not subject to prescription.

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

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{NATURE/TYPE}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Amflee Combo 50 mg/60 mg spot-on solution

2. STATEMENT OF ACTIVE SUBSTANCES

Each 0.5 ml pipette contains:

fipronil	50 mg
s-methoprene	60 mg

3. PACKAGE SIZE

1 x 0.5 ml
3 x 0.5 ml
6 x 0.5 ml
30 x 0.5 ml

4. TARGET SPECIES

Cats.



5. INDICATIONS

For products not subject to veterinary prescription

Kills fleas (*Ctenocephalides spp.*) on treated cats for up to 4 weeks and prevents eggs laid by exposed fleas from developing for up to 6 weeks. Kills ticks (*Ixodes ricinus*, *Dermacentor variabilis*, *Rhipicephalus sanguineus*) on treated cats for up to 2 weeks. Treats infestations with biting lice (*Felicola subrostratus*).



Ctenocephalides felis



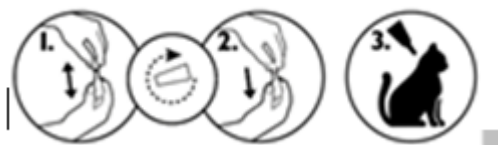
Ixodida



Felicola subrostratus

6. ROUTES OF ADMINISTRATION

Spot-on use.



7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store below 30 °C.

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

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

KRKA, d.d., Novo mesto

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

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

Amflee Combo

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

fipronil /s-methoprene
50 mg/60 mg

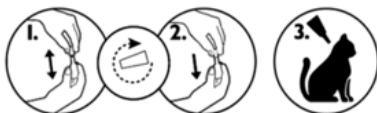
3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

KRKA, d.d., Novo mesto



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

Amflee Combo
Fyperix Combo
Fyperix Comp vet
Fypermid Combo
Fleascreen Combo

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

50 mg/60 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Amflee Combo 50 mg/60 mg spot-on solution for cats

2. Composition

Each 0.5 ml pipette contains:

Active substances:

Fipronil	50 mg
S-Methoprene	60 mg

Excipients:

Butylhydroxyanisole (E320)	0.1 mg
Butylhydroxytoluene (E321)	0.05 mg

Clear yellow solution.

3. Target species

Cats.



4. Indications for use

To be used against infestations with fleas, alone or in association with ticks and/or biting lice:

- Treatment of fleas (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 4 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 six weeks after application.
- Treatment of ticks (*Ixodes ricinus*, *Dermacentor variabilis*, *Rhipicephalus sanguineus*). The veterinary medicinal product has a persistent acaricidal efficacy for up to 2 weeks against ticks (based on experimental data).
- Treatment of biting lice (*Felicola subrostratus*).

5. Contraindications

Do not use on kittens less than 8 weeks old and/or weighing less than 1 kg.

Do not use on sick (e.g. systemic diseases, fever) or convalescent animals.

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

Do not use in rabbits, as adverse drug reactions with even mortality could occur.

Do not use in any other non-target species.

6. Special warnings

Special warnings:

When treating infestations of parasites, all in-contact animals should be treated with an appropriate veterinary medicinal product at the same time. 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.

Bathing and/or shampooing should be avoided. No information on the effect of bathing or the use of a shampoo on the effectiveness of the veterinary medicinal product in cats is available. Based on information available for dogs, 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.

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. There may be an attachment of single ticks. For this reason a transmission of infectious diseases cannot be completely excluded if conditions are unfavourable.

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 (allergy) 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 in clean water.

In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

Do not smoke, drink or eat during application.

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.

Keep pipettes in original packaging until ready to use.

Pregnancy and lactation:

Can be used during pregnancy.

The potential toxicity of the veterinary medicinal product for kittens of less than 8 weeks of age in contact with a treated queen is not documented. Special care should be taken in this case.

Interaction with other medicinal products and other forms of interaction:

Do not use simultaneously with other flea products which are applied directly on to the animal.

Overdose:

The risk of experiencing adverse effects may increase with overdosing (see section "Adverse events").

No undesirable effects were observed in target animal safety studies in cats and kittens aged 8 weeks and older and weighing about 1 kg treated once a month at five times the recommended dose for six consecutive months.

Itching may occur following treatment.

Overdose application of the veterinary medicinal product will cause a sticky appearance of hairs at the treatment spot. However, should this occur, it will disappear within 24 hours post application.

7. Adverse events

Cats:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reactions (skin scaling, localised hair loss, itching, reddening) ¹ Skin and appendages disorders (itching, hair loss)
Undetermined frequency (cannot be estimated from the available data):	Digestive tract disorders (hypersalivation, vomiting) Neurological disorders (increased sensitivity to stimulation, depression, other nervous signs) ²

¹Transient.

²Reversible.

In the case of licking the administration site, 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 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}

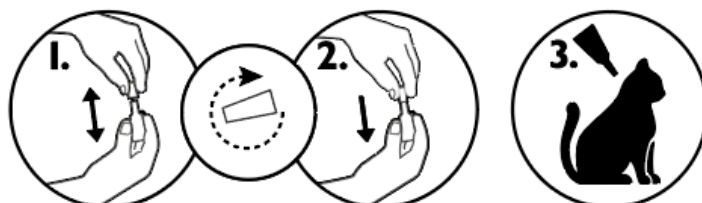
8. Dosage for each species, routes and method of administration

Spot-on use.

One pipette of 0.5 ml per cat, corresponding to a minimum recommended dose of 5 mg/kg for fipronil and 6 mg/kg for (S)-methoprene, by topical application to the skin.

Method of administration:

1. Remove the pipette from its packaging. Hold the pipette in an upright position, twist and pull the cap off.
2. Turn the cap around and place the other end of the cap back on the pipette. Push and twist the cap to break the seal, then remove the cap from the pipette.
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 onto the skin and squeeze the pipette several times to empty its contents completely and directly onto the skin in one spot.



9. Advice on correct administration

In the absence of safety studies, the minimum treatment interval is 4 weeks.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Store below 30 °C.

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

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

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 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 not subject to prescription.

14. Marketing authorisation numbers and pack sizes

White polypropylene single-dose pipette packaged in aluminium foil sachets.

Pack sizes:

Cardboard box containing 1, 3, 6 or 30 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 \(https://medicines.health.europa.eu/veterinary\)](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:

KRKA, d.d., Novo mesto

Šmarješka cesta 6
8501 Novo mesto, Slovenia
Tel.: to be included national

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