ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Seresto 1.25 g + 0.56 g medicated collar for dogs ≤ 8 kg [AT, BE, DE, ES, IT, LU, NL, PT]

Seresto collar small dogs [FR]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each collar of 38 cm (12.5 g) contains:

Active substances:
Imidacloprid 1.25 g
Flumethrin 0.56 g

Excipients:

Qualitative composition of excipients and other constituents
Titanium dioxide (E 171)
Iron oxide black (E 172)
Dibutyladipate
Propylene glycol dicaprylocaprate
Epoxidised soybean oil
Stearic acid
Polyvinyl chloride

Grey, odour free collar embossed with the veterinary medicinal product name on one side.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For dogs with or at risk from mixed infestation by fleas or lice, and ticks or sand flies.
The veterinary medicinal product is only indicated when use against parasites targeted by each of the combined active substances is indicated at the same time.

Treatment of flea infestation and prevention of flea re-infestation (*Ctenocephalides canis, Ctenocephalides felis)* due to insecticidal activity for 7 to 8 months.

Protects the animal's immediate surroundings against flea larvae development for 8 months.

The veterinary medicinal product can be used as part of a treatment strategy for Flea Allergy Dermatitis (FAD) where it has been previously diagnosed by a veterinarian.

Prevention of re-infestation with ticks (*Ixodes ricinus, Rhipicephalus sanguineus)* through acaricidal (killing) effect and through repellent (anti-feeding) effect from 2 days to 8 months.

Prevention of re-infestation with ticks (*Dermacentor reticulatus)* through acaricidal (killing) effect from 2 days to 8 months.

It is effective against larvae, nymphs and adult ticks.

Reduction of the risk of transmission of the pathogens *Babesia canis vogeli* and *Ehrlichia canis*, thereby reducing the risk of canine babesiosis and canine ehrlichiosis for 7 months through acaricidal and repellent effects on the tick vector *Rhipicephalus sanguineus*. The effect is indirect due to product's activity against the vector.

Reduction of the risk of transmission of the pathogen *Leishmania infantum* for up to 8 months, thereby reducing the risk of canine leishmaniosis by repellent activity on sand flies. The effect is indirect due to the product's activity against the vectors.

Treatment of infestation by biting lice (*Trichodectes canis*).

3.3 Contraindications

Do not treat puppies less than 7 weeks of age.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

3.4 Special warnings

Ticks already on the dog prior to treatment may not be killed within 48 hours after collar application and may remain attached and visible. Therefore, removal of ticks already on the dog at the time of application is recommended. The prevention of infestations with new ticks starts within two days after application of the collar.

Ticks will be killed and fall off the host within 24 to 48 hours after infestation without having had a blood meal, as a rule. An attachment of single ticks after treatment cannot be excluded. For this reason, a transmission of infectious diseases by ticks cannot be completely excluded if conditions are unfavourable.

Although a significant reduction in the incidence of *Leishmania infantum* in dogs has been demonstrated, the veterinary medicinal product has shown variable repellent (anti-feeding) and insecticidal efficacy against the sand fly *Phlebotomus perniciosus*. As a result, bites by sand flies may occur, and the transmission of *Leishmania infantum* cannot be completely excluded. The collar should be applied just before the beginning of the period of activity of sand fly vectors corresponding to the *Leishmania infantum* transmission season and worn continuously throughout the risk period.

Ideally, the collar should be applied before the beginning of the flea or tick season.

As in all long term topical veterinary medicinal products, periods of excessive seasonal hair shedding may lead to transient slight reduction of efficacy by loss of hair-bound portions of the active ingredients. Replenishment from the collar starts immediately so that full efficacy will be re-established without any additional treatment or collar replacement.

The possibility that other animals in the same household can be source of re-infestation with fleas, biting lice and ticks should be considered, and these should be treated as necessary with an appropriate product.
For optimal control of flea problems in heavily infested households it may be necessary to treat the environment with a suitable insecticide.
Fleas can infest pets' beds, sleeping areas and usual resting areas like rugs and sofas. In the event of a massive infestation, these places should be treated with a suitable insecticide and vacuumed regularly.

In the absence of risk of co-infestation with fleas, ticks or biting lice, a narrow spectrum veterinary product should be used.

The use of this product should take into account local information about susceptibility of the target parasites, where available. Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.

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 infestation based on its epidemiological features, for each individual animal.
In Europe, resistance to pyrethroids has been reported in an isolated case of *Rhipicephalus sanguineus* in dogs. No resistance of fleas to imidacloprid has been reported so far.

The veterinary medicinal product is water resistant; it remains effective if the animal becomes wet. However, prolonged, intense exposure to water or extensive shampooing should be avoided as the duration of activity may be reduced. Studies show that monthly shampooing or water immersion does not significantly shorten the 8 months efficacy duration for ticks after redistribution of the active substances in the coat whereas the veterinary medicinal product's flea efficacy gradually decreased, starting in the 5th month. The influence of shampooing or water immersion regarding the transmission of canine leishmaniosis has not been examined.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Keep the bag with the collar in the outer packaging until use.
As with any veterinary medicinal products, do not allow small children to play with the collar, or to put it into their mouths. Pets wearing the collar should not be allowed to sleep in the same bed as their owners, especially children. Imidacloprid and flumethrin are continuously released from the collar to the skin and fur whilst the collar is being worn.
The veterinary medicinal product may cause hypersensitivity reactions in some people.
People with known hypersensitivity (allergy) to the ingredients of the collar should avoid contact with the veterinary medicinal product.
The veterinary medicinal product may cause skin, eye and respiratory irritation in some people in very rare cases. In case of eye irritation, flush eyes thoroughly with cold water. In case of skin irritation, wash the skin with soap and cold water. If symptoms persist it is recommended to seek medical advice and show the package leaflet or the label to the physician.
Immediately dispose of any remnants or cut-offs of the collar (see section 3.9).
Wash hands with cold water after fitting the collar.

Special precautions for the protection of the environment:
See section 5.5.

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10 000 animals treated):	Application site reaction[1] (e.g. Erythema, Hair loss, Pruritus, Scratching) Behavioural disorder[2] (e.g. Excessive chewing, licking and grooming[3], Hiding, Hyperactivity, Vocalisation) Diarrhoea[4], Hypersalivation[4], Vomiting[4] Change in food intake[4] Depression[4] Neurological symptoms[5] (e.g. Ataxia, Convulsions, Tremor)

Very rare (< 1 animal / 10 000 animals treated, including isolated reports):	Application site reaction[5] (e.g. Dermatitis, Eczema, Haemorrhage, Inflammation, Lesion) Aggression[6]

[1] Signs usually resolve within 1 to 2 weeks. In single cases, temporary collar removal is recommended until signs resolve.
[2] May be observed in animals that are not used to wearing collars on the first few days after fitting.
[3] At the application site.
[4] Slight and transient reactions that might occur with initial use.
[5] In these cases, collar removal is recommended.
[6] Ensure that collar is fitted correctly.

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

The safety of the veterinary medicinal product has not been established in target animals during pregnancy and lactation.

Pregnancy and lactation:
The use is not recommended during pregnancy and lactation.
Laboratory studies with either flumethrin or imidacloprid in rats and rabbits showed no teratogenic, or foetotoxic effects.

Fertility:
Laboratory studies with either flumethrin or imidacloprid in rats and rabbits have not produced any effects on fertility or reproduction.

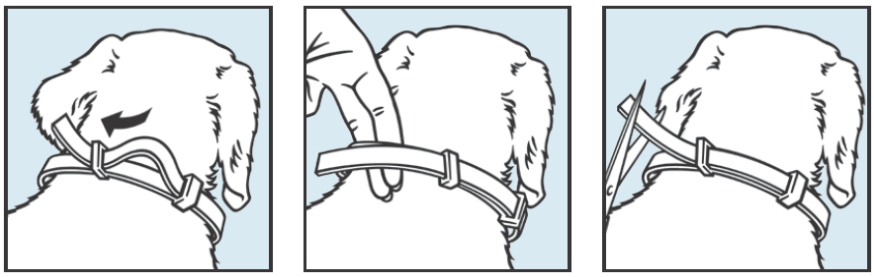
3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cutaneous use. One collar per animal to be fastened around the neck.
Small dogs up to 8 kg body weight receive one collar of 38 cm length.
Underdosing could result in ineffective use and may favour resistance development. To ensure a correct dosage, body weight should be determined as accurately as possible.
For external use only.

Remove collar from protective bag directly before use. Unroll collar and make sure that there are no remnants from the plastic connectors inside the collar. Pull the collar through the buckle and adjust it around the animal's neck without tightening it too tight (as a guide, it should be possible to insert 2 fingers between the collar and the neck). Pull excess collar through the loop and cut off any excess length extending beyond 2 cm.



The collar should be worn continuously for the 8 month protection period and should be removed after the treatment period. Check periodically and adjust fit if necessary, especially when puppies are rapidly growing.

This collar is designed with a safety-closure mechanism. In the extremely rare event of a dog being trapped, the animals own strength is usually sufficient to widen the collar to allow for quick release.

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

Due to the nature of the collar overdosage is unlikely and signs of overdosage are not to be expected. An overdosage of 5 collars around the neck was investigated in adult dogs for an 8 months period and in 7 week old puppies for a 6 months period and no adverse effects were observed besides slight hair loss and mild skin reactions.
In the unlikely event of the animal eating the collar mild gastrointestinal symptoms (e.g. loose stool) may occur.

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 : QP53AC55.

4.2 Pharmacodynamics

Imidacloprid is an ectoparasiticide belonging to the chloronicotinyl group of compounds. Chemically, it can be classified as a chloronicotinyl nitroguanidine. Imidacloprid is active against larval flea stages, adult fleas and lice. Efficacy against fleas (*Ctenocephalides felis* and *Ctenocephalides canis*) starts within 48 hours after application of the collar. In addition to the indications listed under section 3.2 an activity against *Pulex irritans* fleas has been demonstrated.

Imidacloprid has a high affinity for the nicotinergic acetylcholine receptors in the post-synaptic region of the central nervous system (CNS) of the flea. The ensuing inhibition of cholinergic transmission in insects results in paralysis and death. Due to the weak nature of the interaction with mammalian nicotinergic receptors and the postulated poor penetration through the blood-brain barrier in mammals, it has virtually no effect on the mammalian CNS. Imidacloprid has minimal pharmacological activity in mammals.

Flumethrin is an ectoparasiticide of the synthetic pyrethroid group. According to current knowledge the synthetic pyrethroids interfere with the sodium channel of nerve cell membranes, resulting in a delay in repolarization of the nerve and finally killing of the parasite. In studies on structure-activity relationship of a number of pyrethroids interference with receptors of a certain chiral conformation was noted thereby causing a selective activity on ectoparasites. No anti-cholinesterase activity was noted with these compounds. Flumethrin is responsible for the veterinary medicinal product's acaricidal activity and also prevents production of fertile eggs by its lethal effect on female ticks. In an *in-vitro* study 5 to 10 % of *Rhipicephalus sanguineus* ticks exposed to a sublethal dose of 4 mg flumethrin/L laid eggs which had a modified appearance (shrivelled, dull and dry) indicating a sterilising effect. According to current knowledge resistance is conferred by gene mutations at the target site as well as increased metabolic detoxification.

In addition to the tick species listed under section 3.2 activity has been demonstrated against *Ixodes hexagonus, I. scapularis* and the non-European tick species *Dermacentor variabilis* and the Australian paralysis tick *I. holocyclus*.

The veterinary medicinal product provides repellent (anti-feeding) activity against the claimed ticks, thus preventing repelled parasites from taking a blood meal and thereby indirectly aids in the reduction of the risk of Canine Vector-Borne Disease transmission.
In addition to the pathogens listed in section 3.2, indirect protection against the transmission of *Babesia canis canis* (by *Dermacentor reticulatus* ticks) has been shown in one laboratory study at day 28 after treatment, and indirect protection against the transmission of *Anaplasma phagocytophilum* (by *Ixodes ricinus* ticks) has been shown in one laboratory study at 2 months after treatment, thereby reducing the risk of diseases caused by these pathogens under the conditions of these studies.

Data from efficacy studies against sand flies (*Phlebotomus perniciosus*) showed a variable sand fly repellent (anti-feeding) efficacy ranging from 65 to 89% for 7-8 months following initial application of the collar. Data from 3 clinical field studies performed in endemic areas indicate a significant reduction in the risk of *Leishmania infantum* transmission by sand flies in treated dogs compared to non-treated dogs. Depending on the infection pressure by sand flies the efficacy in the reduction of the risk of infection with leishmaniosis ranged from 88.3 to 100%.

The collars were able to improve the *Sarcoptes scabiei* infestation in pre-infested dogs leading to a full cure after three months.

4.3 Pharmacokinetics

Both active ingredients are slowly and continuously released in low concentrations from the polymer matrix system of the collar towards the animal. Both actives are present in the dog's haircoat in acaricidal/insecticidal concentrations during the entire efficacy period. The active substances spread from the site of direct contact over the entire skin surface. Target animal overdose and serum kinetic studies have established that imidacloprid reached the systemic circulation transiently while flumethrin was mostly not measurable. Oral absorption of both active substances is not relevant for the clinical efficacy.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 5 years.

5.3 Special precautions for storage

Keep the bag with the collar in the outer box until use.

5.4 Nature and composition of immediate packaging

Box containing one single or two 38 cm polyvinyl chloride based collar(s) individually packed into a PETP/PE bag.
Carton pack containing twelve 38 cm polyvinyl chloride based collars individually packed into a PETP/PE bag.
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 imidacloprid and flumethrin 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

Elanco

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF 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. (BE)
Veterinary medicinal product not subject to prescription. (AT, DE, ES, FR, IT, LU, NL, PT)

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

Box or carton pack

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Seresto 1.25 g + 0.56 g medicated collar

2. STATEMENT OF ACTIVE SUBSTANCES

Each collar contains: 1.25 g imidacloprid, 0.56 g flumethrin.

Grey, odour free collar.

3. PACKAGE SIZE

1 x 38 cm collar
2 x 38 cm collar
12 x 38 cm collar

4. TARGET SPECIES

Dogs (≤ 8 kg).

5. INDICATIONS

For products not subject to veterinary prescription

Kills ticks, fleas and lice and repels ticks ("anti-feeding"). Indirect protection against transmission of canine vector-borne disease pathogens (e.g.*leishmaniosis, ehrlichiosis, babesiosis)*. 7-8 months protection. Water resistant veterinary medicinal product.

 Tick  Flea  Larvae  Louse

6. ROUTES OF ADMINISTRATION

Cutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Keep the bag with the collar in the outer box until use.

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

Elanco logo

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

PETP/PE bag

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Seresto 1.25 g + 0.56 g medicated collar

2. STATEMENT OF ACTIVE SUBSTANCES

Each collar contains: 1.25 g imidacloprid, 0.56 g flumethrin.

3. TARGET SPECIES

Dogs (≤ 8 kg).

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Cutaneous use.

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Exp. {mm/yyyy}

7. SPECIAL STORAGE PRECAUTIONS

Keep the bag with the collar in the outer box until use.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco logo

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Seresto 1.25 g + 0.56 g medicated collar for dogs ≤ 8 kg

2. Composition

Each grey, odour free collar of 38 cm (12.5 g) contains 1.25 g imidacloprid and 0.56 g flumethrin as active substances and is embossed with the veterinary medicinal product name on one side.

3. Target species

Dogs.

4. Indications for use

For dogs with or at risk from mixed infestation by fleas or lice, and ticks or sand flies.
The veterinary medicinal product is only indicated when use against parasites targeted by each of the combined active substances is indicated at the same time.

Treatment of flea infestation and prevention of flea re-infestation (*Ctenocephalides canis, Ctenocephalides felis)* due to insecticidal activity for 7 to 8 months.

Protects the animal's immediate surroundings against flea larvae development for 8 months.

The veterinary medicinal product can be used as part of a treatment strategy for Flea Allergy Dermatitis (FAD) where it has been previously diagnosed by a veterinarian.

Prevention of re-infestation with ticks (*Ixodes ricinus, Rhipicephalus sanguineus)* through acaricidal (killing) effect and through repellent (anti-feeding) effect from 2 days to 8 months.

Prevention of re-infestation with ticks (*Dermacentor reticulatus)* through acaricidal (killing) effect from 2 days to 8 months.

It is effective against larvae, nymphs and adult ticks.

Reduction of the risk of transmission of the pathogens *Babesia canis vogeli* and *Ehrlichia canis*, thereby reducing the risk of canine babesiosis and canine ehrlichiosis for 7 months through acaricidal and repellent effects on the tick vector *Rhipicephalus sanguineus*. The effect is indirect due to product's activity against the vector.

Reduction of the risk of transmission of the pathogen *Leishmania infantum* for up to 8 months, thereby reducing the risk of canine leishmaniosis by repellent activity on sand flies. The effect is indirect due to the product's activity against the vectors.

Treatment of infestation by biting lice (*Trichodectes canis*).

5. Contraindications

Do not treat puppies less than 7 weeks of age.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

6. Special warnings

Special warnings:
Ticks already on the dog prior to treatment may not be killed within 48 hours after collar application and may remain attached and visible. Therefore, removal of ticks already on the dog at the time of application is recommended. The prevention of infestations with new ticks starts within two days after application of the collar.

Ticks will be killed and fall off the host within 24 to 48 hours after infestation without having had a blood meal, as a rule. An attachment of single ticks after treatment cannot be excluded. For this reason, a transmission of infectious diseases by ticks cannot be completely excluded if conditions are unfavourable.

Although a significant reduction in the incidence of *Leishmania infantum* in dogs has been demonstrated, the veterinary medicinal product has shown variable repellent (anti-feeding) and insecticidal efficacy against the sand fly *Phlebotomus perniciosus*. As a result, bites by sand flies may occur, and the transmission of *Leishmania infantum* cannot be completely excluded. The collar should be applied just before the beginning of the period of activity of sand fly vectors corresponding to the *Leishmania infantum* transmission season and worn continuously throughout the risk period.

Ideally, the collar should be applied before the beginning of the flea or tick season.

As in all long term topical veterinary medicinal products, periods of excessive seasonal hair shedding may lead to transient slight reduction of efficacy by loss of hair-bound portions of the active ingredients. Replenishment from the collar starts immediately so that full efficacy will be re-established without any additional treatment or collar replacement.

The possibility that other animals in the same household can be source of re-infestation with fleas, biting lice and ticks should be considered, and these should be treated as necessary with an appropriate product.
For optimal control of flea problems in heavily infested households it may be necessary to treat the environment with a suitable insecticide.
Fleas can infest pets' beds, sleeping areas and usual resting areas like rugs and sofas. In the event of a massive infestation, these places should be treated with a suitable insecticide and vacuumed regularly.

In the absence of risk of co-infestation with fleas, ticks or biting lice, a narrow spectrum veterinary product should be used.

The use of this product should take into account local information about susceptibility of the target parasites, where available. Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.

Unnecessary use of antiparasitics or use deviating from the instructions given in the package leaflet 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 infestation based on its epidemiological features, for each individual animal.
In Europe, resistance to pyrethroids has been reported in an isolated case of *Rhipicephalus sanguineus* in dogs. No resistance of fleas to imidacloprid has been reported so far.

The veterinary medicinal product is water resistant; it remains effective if the animal becomes wet. However, prolonged, intense exposure to water or extensive shampooing should be avoided as the duration of activity may be reduced. Studies show that monthly shampooing or water immersion does not significantly shorten the 8 months efficacy duration for ticks after redistribution of the active substances in the coat whereas the veterinary medicinal product's flea efficacy gradually decreased,

starting in the 5th month. The influence of shampooing or water immersion regarding the transmission of canine leishmaniosis has not been examined.

Special precautions for safe use in the target species:
Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Keep the bag with the collar in the outer packaging until use.
As with any veterinary medicinal product, do not allow small children to play with the collar, or to put it into their mouths. Pets wearing the collar should not be allowed to sleep in the same bed as their owners, especially children. Imidacloprid and flumethrin are continuously released from the collar to the skin and fur whilst the collar is being worn.
The veterinary medicinal product may cause hypersensitivity reactions in some people.
People with known hypersensitivity (allergy) to the ingredients of the collar should avoid contact with the veterinary medicinal product.
The veterinary medicinal product may cause skin, eye and respiratory irritation in some people in very rare cases. In case of eye irritation, flush eyes thoroughly with cold water. In case of skin irritation, wash the skin with soap and cold water. If symptoms persist it is recommended to seek medical advice and show the package leaflet or the label to the physician.
Immediately dispose of any remnants or cut-offs of the collar (see section "advice on correct administration").
Wash hands with cold water after fitting the collar.

Special precautions for the protection of the environment:
See section, "Special Precautions for Disposal".

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in target animals during pregnancy and lactation. The use is not recommended during pregnancy and lactation.
Laboratory studies with either flumethrin or imidacloprid in rats and rabbits showed no teratogenic, or foetotoxic effects.

Fertility:
Laboratory studies with either flumethrin or imidacloprid in rats and rabbits have not produced any effects on fertility or reproduction.

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

Overdose:
Due to the nature of the collar overdosage is unlikely and signs of overdosage are not to be expected.
An overdosage of 5 collars around the neck was investigated in adult dogs for an 8 months period and in 7 week old puppies for a 6 months period and no adverse effects were observed besides slight hair loss and mild skin reactions.
In the unlikely event of the animal eating the collar mild gastrointestinal symptoms (e.g. loose stool) may occur.

Major incompatibilities:
None known.

7. Adverse events

Dogs:

Rare (1 to 10 animals / 10 000 animals treated):	Application site reaction[1] (e.g. Erythema (redness), Hair loss, Pruritus (itching), Scratching) Behavioural disorder[2] (e.g. Excessive chewing, licking and grooming[3], Hiding, Hyperactivity, Vocalisation) Diarrhoea[4], Hypersalivation[4] (increased salivation), Vomiting[4] Change in food intake[4] Depression[4] Neurological symptoms[5] (e.g. Ataxia (incoordination), Convulsions, Tremor)
Very rare (< 1 animal / 10 000 animals treated, including isolated reports):	Application site reaction[5] (e.g. Dermatitis, Eczema, Haemorrhage, Inflammation, Lesion) Aggression[6]

[1] Signs usually resolve within 1 to 2 weeks. In single cases, temporary collar removal is recommended until signs resolve.
[2] May be observed in animals that are not used to wearing collars on the first few days after fitting.
[3] At the application site.
[4] Slight and transient reactions that might occur with initial use.
[5] In these cases, collar removal is recommended.
[6] Ensure that collar is fitted correctly.

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

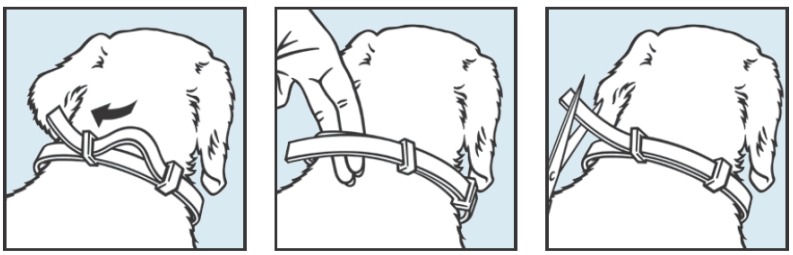
Cutaneous use. One collar per animal to be fastened around the neck.
Small dogs up to 8 kg receive one collar of 38 cm length.

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

9. Advice on correct administration

Remove collar from protective bag directly before use. Unroll collar and make sure that there are no remnants from the plastic connectors inside the collar. Pull the collar through the buckle and adjust it around the animal's neck without tightening it too tight (as a guide, it should be possible to insert 2 fingers between the collar and the neck). Pull excess collar through the loop and cut off any excess length extending beyond 2 cm.

For multilingual packaging only:
<See illustration of collar use at the end of this leaflet. >



The collar should be worn continuously for the 8 month protection period and should be removed after the treatment period. Check periodically and adjust fit if necessary, especially when puppies are rapidly growing.

This collar is designed with a safety-closure mechanism. In the extremely rare event of a dog being trapped, the animals own strength is usually sufficient to widen the collar to allow for quick release.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Keep the bag with the collar in the outer box until use.
Do not use after expiry date stated on the bag and outer box. 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 imidacloprid and flumethrin 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. (BE)
Veterinary medicinal product not subject to prescription. (AT, DE, ES, FR, IT, LU, NL, PT)

14. Marketing authorisation numbers and pack sizes

Box containing one or two collars; carton containing 12 collars.
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 events:

Manufacturer responsible for batch release:
KVP Pharma + Veterinär Produkte GmbH, Projensdorfer Str. 324, 24106 Kiel, Germany

Local representatives and contact details to report suspected adverse events:

17. Other information

Both active ingredients are slowly and continuously released in low concentrations from the polymer matrix system of the collar towards the animal. Both actives are present in the dog's haircoat in acaricidal/insecticidal concentrations during the entire efficacy period. The active substances spread from the site of direct contact over the entire skin surface. Target animal overdose and serum kinetic studies have established that imidacloprid reached the systemic circulation transiently while flumethrin was mostly not measurable. Oral absorption of both active substances is not relevant for the clinical efficacy.

Efficacy against fleas (*Ctenocephalides felis* and *Ctenocephalides canis*) starts within 48 hours after application of the collar. In addition to the indications listed above an activity against *Pulex irritans* fleas has been demonstrated.
In addition to the tick species listed above activity has been demonstrated against *Ixodes hexagonus, I. scapularis* and the non-European tick species *Dermacentor variabilis* and the Australian paralysis tick *I. holocyclus*.
The veterinary medicinal product provides repellent (anti-feeding) activity against the claimed ticks, thus preventing repelled parasites from taking a blood meal and thereby indirectly aids in the reduction of the risk of Canine Vector-Borne Disease transmission. In addition to the pathogens listed under indications, indirect protection against the transmission of *Babesia canis canis* (by *Dermacentor reticulatus* ticks) has been shown in one laboratory study at day 28 after treatment, and indirect protection against the transmission of *Anaplasma phagocytophilum* (by *Ixodes ricinus* ticks) has been shown in one laboratory study at 2 months after treatment, thereby reducing the risk of diseases caused by these pathogens under the conditions of these studies.

Data from efficacy studies against sand flies (*Phlebotomus perniciosus*) showed a variable sand fly repellent (anti-feeding) efficacy ranging from 65 to 89% for 7-8 months following initial application of the collar. Data from 3 clinical field studies performed in endemic areas indicate a significant reduction in the risk of *Leishmania infantum* transmission by sand flies in treated dogs compared to non-treated dogs. Depending on the infection pressure by sand flies the efficacy in the reduction of the risk of infection with leishmaniosis ranged from 88.3 to 100%.

The collars were able to improve the *Sarcoptes scabiei* infestation in pre-infested dogs leading to a full cure after three months.