ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Lotilaner/Milbemycin Elanco 56.25 mg/2.11 mg chewable tablets for dogs (1.4-2.8 kg)
Lotilaner/Milbemycin Elanco 112.5 mg/4.22 mg chewable tablets for dogs (> 2.8-5.5 kg)
Lotilaner/Milbemycin Elanco 225 mg/8.44 mg chewable tablets for dogs (> 5.5-11 kg)
Lotilaner/Milbemycin Elanco 450 mg/16.88 mg chewable tablets for dogs (> 11-22 kg)
Lotilaner/Milbemycin Elanco 900 mg/33.75 mg chewable tablets for dogs (> 22-45 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Active substances:	**Lotilaner**	**Milbemycin oxime**
Dogs (1.4-2.8 kg)	56.25 mg	2.11 mg
Dogs (> 2.8-5.5 kg)	112.5 mg	4.22 mg
Dogs (> 5.5-11 kg)	225 mg	8.44 mg
Dogs (> 11-22 kg)	450 mg	16.88 mg
Dogs (> 22-45 kg)	900 mg	33.75 mg

Excipients:

Qualitative composition of excipients and other constituents
Cellulose, powdered
Lactose monohydrate
Silicified microcrystalline cellulose
Meat dry flavour
Crospovidone
Povidone K30
Sodium laurilsulfate
Silica, colloidal anhydrous
Magnesium stearate

White to beige round biconvex chewable tablet with brownish spots and bevelled edges with letter “I” debossed on one side of the tablet.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For use in dogs with, or at risk from, mixed infestations/infections by ticks, fleas, mites, gastrointestinal nematodes, heartworm and/or lungworm. This veterinary medicinal product is only indicated for use when treatment against ticks/fleas/mites and gastrointestinal nematodes or the treatment against ticks/fleas/mites and prevention of heartworm disease/angiostrongylosis is indicated at the same time.

Ectoparasites
For the treatment of tick (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus* and *I. hexagonus*) and flea (*Ctenocephalides felis* and *C. canis*) infestations in dogs.

This veterinary medicinal product provides immediate and persistent killing activity for 1 month for ticks and fleas.

The veterinary medicinal product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

For reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for one month. The effect is indirect due to the activity of the veterinary medicinal product against the vector.

For the treatment of demodicosis (caused by *Demodex canis*).

For the treatment of sarcoptic mange (*Sarcoptes scabiei* var. *canis*).

Gastrointestinal Nematodes
Treatment of gastrointestinal nematodes: hookworm (L4, immature adult (L5) and adult *Ancylostoma caninum*), roundworms (L4, immature adult (L5) and adult *Toxocara canis*, and adult *Toxascaris leonina*) and whipworm (adult *Trichuris vulpis*).

Heartworm
Prevention of heartworm disease (*Dirofilaria immitis*).

Lungworm
Prevention of angiostrongylosis by reduction of the level of infection with immature adult (L5) and adult stages of *Angiostrongylus vasorum* (lungworm) with monthly administration.

3.3 Contraindications

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

3.4 Special warnings

The possibility that other animals in the same household can be a source of re-infection with ticks, fleas, mites, gastrointestinal nematodes, heartworm and/or lungworm should be considered, and these should be treated as necessary with an appropriate product.

The product should be used in dogs with, or at risk from, mixed infestations of ectoparasites (ticks, fleas or mites) and endoparasites (gastrointestinal nematodes and/or for prevention of heartworm/lungworm). In the absence of risk of co-infestation by external and internal parasites, a narrow spectrum product should be used.

Ticks and fleas must attach to the host and commence feeding in order to be exposed to the active substance; therefore, the risk of the transmission of tick/flea-borne diseases cannot be excluded. Specifically, as an acaricidal effect against *D. reticulatus* may take up to 48 hours, transmission of *B. canis canis* during the first 48 hours cannot be excluded.

For the treatment of infections with gastrointestinal nematodes the need for, and the frequency of, re-treatment as well as the choice of the treatment (monosubstance or combination product) should be evaluated by the prescribing veterinarian.

Maintenance of the efficacy of macrocyclic lactones is critical for *Dirofilaria immitis* prevention, therefore, to minimise the risk of resistance selection, it is recommended that dogs should be checked for both circulating antigens and blood microfilariae at the beginning of each heartworm season prior

to starting monthly preventive treatments. The product is not effective against adult *D. immitis* and is not indicated for microfilariae clearance.

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 infection/infestation based on its epidemiological features, for each individual animal.

3.5 Special precautions for use

Special precautions for safe use in the target species:
All safety and efficacy data have been acquired from dogs and puppies 8 weeks of age and older and 1.4 kg of bodyweight and greater. Use of this veterinary medicinal product in puppies younger than 8 weeks of age or less than 1.4 kg of bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

The recommended dose should be strictly observed in MDR1 mutant ($^{-/-}$) dogs with a non-functional P-glycoprotein, which may include Collies and related breeds.

Prior to first administration, dogs in heartworm endemic areas or who have visited heartworm endemic areas must be tested for existing heartworm infection. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to kill adult heartworms.

Administration of products containing milbemycin oxime (such as this product) to dogs with a high number of circulating microfilariae is not recommended in order to avoid hypersensitivity reactions associated with the release of proteins from dead or dying microfilariae.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Accidental ingestion may cause gastrointestinal disturbances. In order to prevent access by children, keep the chewable tablets in the blister packs until required and keep the blister packs in the outer carton out of the reach of children.

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

Wash hands after handling the tablets.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Uncommon (1 to 10 animals / 1 000 animals treated):	Behavioural disorder [1,2] Diarrhoea[2], Vomiting[2] Muscle tremor[2] Pruritus[2] Anorexia[2], Lethargy[2]
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Ataxia[3], Convulsion[3], Muscle tremor[3]

[1] Changes in behaviour.
[2] Generally self-limiting and of short duration.
[3] These signs typically resolve without treatment.

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 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 during pregnancy or lactation or in breeding dogs.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy or lactation. Laboratory studies in rats have not produced any evidence of teratogenic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

Fertility:
The safety of the veterinary medicinal product has not been established in breeding dogs. Laboratory studies in rats have not produced any evidence of any adverse effect on the reproductive capacity of males and females. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Lotilaner and milbemycin oxime have been shown to be a substrate for P-glycoprotein (P-gp) and therefore could interact with other P-gp substrates (e.g. digoxin, doxorubicin) or other macrocyclic lactones. Therefore, concomitant treatment with other P-gp substrates could lead to enhanced toxicity.

3.9 Administration routes and dosage

Oral use.

The veterinary medicinal product should be administered in accordance with the following table to ensure a dose of 20 to 41 mg lotilaner/kg bodyweight and 0.75 to 1.53 mg milbemycin oxime/kg bodyweight.

Dog bodyweight	**Strength and number of Lotilaner/Milbemycin Elanco chewable tablets to be administered**				
	56.25 mg/ 2.11 mg	112.5 mg/ 4.22 mg	225 mg/ 8.44 mg	450 mg/ 16.88 mg	900 mg/ 33.75 mg
1.4-2.8 kg	1				
> 2.8-5.5 kg		1			
> 5.5-11 kg			1		
> 11-22 kg				1	
> 22-45 kg					1
> 45 kg	Appropriate combination of tablets				

Use an appropriate combination of available strengths to achieve the recommended dose of 20-41 mg lotilaner/kg and 0.75-1.53 mg milbemycin oxime/kg for animals > 45 kg bodyweight. 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 infestations/infections with parasites, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle. If based on the veterinarian's opinion the dog requires re-administration(s) of the product, any subsequent administration(s) must follow the 1-month interval schedule.

Method of administration:
The veterinary medicinal product is a palatable chewable flavoured tablet. Administer the chewable tablet(s) with or after food.

Dogs living in non-heartworm endemic areas:
The veterinary medicinal product can be used as part of the seasonal treatment of ticks and/or fleas in dogs with diagnosed, or at risk from, concurrent gastrointestinal nematode infections or at risk of lungworm. A single treatment is effective for the treatment of gastrointestinal nematodes.

Dogs living in heartworm endemic areas:
Prior to treatment with the veterinary medicinal product the advice in sections 3.4 and 3.5 should be considered.

For the prevention of heartworm disease and the concurrent treatment of tick and/or flea infestations, the veterinary medicinal product must be given at regular monthly intervals during the time of the year when mosquitoes, ticks and/or fleas are present. The first dose of the veterinary medicinal product may be given after first possible exposure to mosquitoes, but not more than one month after this exposure.

When the veterinary medicinal product is used to replace another heartworm preventive product, the first dose of the product must be given within a month of the last dose of the former medication. Dogs travelling to a heartworm region should start medication within a month after arrival there. Heartworm prevention treatment should be continued monthly, with the last administration being given 1 month after the dog has left the region.

Lungworm:
In endemic areas, monthly administration of the veterinary medicinal product will reduce the level of infection with immature adults (L5) and adults of *Angiostrongylus vasorum* in the heart and lungs. It is recommended that lungworm prevention should be continued until at least 1 month after the last exposure to slugs and snails.

Seek veterinary advice regarding information on the optimal time to start treatment with this veterinary medicinal product.

For the treatment of demodicosis (caused by *Demodex canis*):
Monthly administration of the product for two consecutive months is efficacious and leads to a marked improvement of clinical signs. Treatment should be continued until two negative skin scrapings are obtained one month apart. Severe cases may require prolonged monthly treatments. As demodicosis is a multi-factorial disease, where possible, it is advisable to also treat any underlying disease appropriately.

For the treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*):
Monthly administration of the product for two consecutive months. Further monthly administration of the product may be required based on clinical assessment and skin scrapings.

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

No adverse reactions, other than those listed in section 3.6, were observed in puppies (starting at 8-9 weeks of age) after administering up to 5 times the maximum recommended dose over 1-5 days (consecutive daily dosing) at monthly intervals on 9 occasions; or in adult dogs (starting at 11 months of age) after administering up to 5 times the maximum recommended dose over 1-5 days (consecutive daily dosing) at monthly intervals on 7 occasions; or in adult dogs (approximately 12 months old) after administration up to 6 times the maximum recommended dose as a bolus on a single occasion.

After administration of 5 times the maximum recommended dose to MDR1 mutant ($^{-/-}$) dogs with a non-functional P-glycoprotein, transient depression, ataxia, tremors, mydriasis and/or excessive salivation were observed.

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 :

QP54AB51

4.2 Pharmacodynamics

Lotilaner:
Lotilaner is an insecticide and acaricide of the isoxazoline family. It is a pure enantiomer that is active against adult ticks such as *Dermacentor reticulatus, Ixodes hexagonus, I. ricinus and Rhipicephalus sanguineus* as well as adult fleas such as *Ctenocephalides felis* and *C. canis* as well as *Demodex canis* and *Sarcoptes scabiei* var. *canis* mites.

Lotilaner is a potent inhibitor of gamma–aminobutyric acid (GABA)-gated chloride channels and to a lesser extent of glutamate-gated chloride ion channels of insects and ticks, resulting in rapid death of ticks and fleas. The activity of lotilaner has not been found to be affected by resistance to organochlorines (cyclodienes, e.g. dieldrin), phenylpyrazoles (e.g. fipronil), neonicotinoids (e.g. imidacloprid), formamidines (e.g. amitraz) and pyrethroids (e.g. cypermethrin).

For ticks, the onset of efficacy is within 48 hours of attachment for one month after product administration. Existing *I. ricinus* ticks present on the dog prior to administration are killed within 8 hours.

For fleas, the onset of efficacy is within 4 hours of being infested for one month after product administration. Fleas present on the dog prior to administration are killed within 6 hours.

The veterinary medicinal product kills existing and newly emerged flea infestations on dogs before the female can lay eggs. Therefore, the product breaks the flea life cycle and prevents environmental flea contamination in areas to which the dog has access.

Milbemycin oxime:
Milbemycin oxime is a systemically active macrocyclic lactone isolated from the fermentation of *Streptomyces hygroscopicus var. aureolacrimosus.* It contains two major factors, A3 and A4 (ratio of A3:A4 is 20:80). Milbemycin oxime is an antiparasitic endectocide with activity against mites, larval and adult stages of nematodes as well as larvae (L3/L4) of *Dirofilaria immitis*.

The activity of milbemycin oxime is related to its action on invertebrate neurotransmission. Milbemycin oxime, like avermectins and other milbemycins, increases nematode and insect membrane permeability to chloride ions via glutamate-gated chloride ion channels. This leads to hyperpolarisation of the neuromuscular membrane and flaccid paralysis and death of the parasite.

4.3 Pharmacokinetics

Absorption

Lotilaner is readily absorbed following oral administration and peak plasma concentration is reached within 3-5 hours. Milbemycin A3 5-oxime and milbemycin A4 5-oxime are also rapidly absorbed following oral administration with a T_{max} of approximately 2-4 hours for each drug substance. Food enhances the absorption of both lotilaner and milbemycin oxime. The bioavailability of lotilaner is 75% and that of milbemycin (A_3 and A_4 5-oximes) is approximately 60%.

Distribution
Lotilaner and milbemycin A3 and A4 5-oximes are extensively distributed in dogs where volume of distribution after intravenous administration is 3-4 L/kg. Plasma protein binding is high for both lotilaner and milbemycin oxime (> 95%).

Metabolism and Excretion
Lotilaner is metabolized to a small extent into more hydrophilic compounds which are observed in faeces and urine.

The major route of elimination for lotilaner is biliary excretion, with renal excretion being the minor route of elimination (less than 10% of the dose). The terminal half-life is approximately 24 days. This long terminal half-life provides effective blood concentrations for the entire duration of the inter-dosing interval. With repeated monthly doses, slight accumulation is observed with steady state being reached after the fourth monthly dose.

The primary faecal and urinary metabolites of milbemycin oxime in dog were identified as glucuronide conjugates of milbemycin A3 or A4 5-oximes, dealkylated milbemycin A3 or A4 5-oximes, and hydroxylated milbemycin A4 5-oxime. Hydroxymilbemycin A4 5-oxime was detected only in plasma, but not in urine or faeces, suggesting predominant excretion of conjugated metabolites in the dog.

Milbemycin A4 5-oxime eliminates more slowly than milbemycin A3 5-oxime (clearance after intravenous administration was 47.0 and 106.8 mL/h/kg, respectively) resulting in exposure (AUC) to milbemycin A4 that is higher than to milbemycin A3 5-oxime. The mean elimination half-lives were 27 hours for A3 and 57 hours for A4. Excretion of milbemycin A3 and A4 5-oxime is primarily via faeces, and to a lesser extent in the urine.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

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

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

Aluminium/aluminium blisters packaged into an outer cardboard box.
Pack sizes of 1, 3, 6 or 18 tablets.

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.

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)

EU/2/26/361/001-020

8. DATE OF FIRST AUTHORISATION

25/02/2026

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

DD month YYYY

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

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

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Lotilaner/Milbemycin Elanco 56.25 mg/2.11 mg chewable tablets (1.4-2.8 kg)
Lotilaner/Milbemycin Elanco 112.5 mg/4.22 mg chewable tablets (> 2.8-5.5 kg)
Lotilaner/Milbemycin Elanco 225 mg/8.44 mg chewable tablets (> 5.5-11 kg)
Lotilaner/Milbemycin Elanco 450 mg/16.88 mg chewable tablets (> 11-22 kg)
Lotilaner/Milbemycin Elanco 900 mg/33.75 mg chewable tablets (> 22-45 kg)

2. STATEMENT OF ACTIVE SUBSTANCES

56.25 mg lotilaner / 2.11 mg milbemycin oxime
112.5 mg lotilaner / 4.22 mg milbemycin oxime
225 mg lotilaner / 8.44 mg milbemycin oxime
450 mg lotilaner / 16.88 mg milbemycin oxime
900 mg lotilaner / 33.75 mg milbemycin oxime

3. PACKAGE SIZE

1 tablet
3 tablets
6 tablets
18 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.
Administer with or after food.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

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

EU/2/26/361/001 (56.25 mg lotilaner + 2.11 mg milbemycin oxime; 1 chewable tablet)
EU/2/26/361/002 (56.25 mg lotilaner + 2.11 mg milbemycin oxime; 3 chewable tablets)
EU/2/26/361/003 (56.25 mg lotilaner + 2.11 mg milbemycin oxime; 6 chewable tablets)
EU/2/26/361/004 (56.25 mg lotilaner + 2.11 mg milbemycin oxime; 18 chewable tablets)
EU/2/26/361/005 (112.5 mg lotilaner + 4.22 mg milbemycin oxime; 1 chewable tablet)
EU/2/26/361/006 (112.5 mg lotilaner + 4.22 mg milbemycin oxime; 3 chewable tablets)
EU/2/26/361/007 (112.5 mg lotilaner + 4.22 mg milbemycin oxime; 6 chewable tablets)
EU/2/26/361/008 (112.5 mg lotilaner + 4.22 mg milbemycin oxime; 18 chewable tablets)
EU/2/26/361/009 (225 mg lotilaner + 8.44 mg milbemycin oxime; 1 chewable tablet)
EU/2/26/361/010 (225 mg lotilaner + 8.44 mg milbemycin oxime; 3 chewable tablets)
EU/2/26/361/011 (225 mg lotilaner + 8.44 mg milbemycin oxime; 6 chewable tablets)
EU/2/26/361/012 (225 mg lotilaner + 8.44 mg milbemycin oxime; 18 chewable tablets)
EU/2/26/361/013 (450 mg lotilaner + 16.88 mg milbemycin oxime; 1 chewable tablet)
EU/2/26/361/014 (450 mg lotilaner + 16.88 mg milbemycin oxime; 3 chewable tablets)
EU/2/26/361/015 (450 mg lotilaner + 16.88 mg milbemycin oxime; 6 chewable tablets)
EU/2/26/361/016 (450 mg lotilaner + 16.88 mg milbemycin oxime; 18 chewable tablets)
EU/2/26/361/017 (900 mg lotilaner + 33.75 mg milbemycin oxime; 1 chewable tablet)
EU/2/26/361/018 (900 mg lotilaner + 33.75 mg milbemycin oxime; 3 chewable tablets)
EU/2/26/361/019 (900 mg lotilaner + 33.75 mg milbemycin oxime; 6 chewable tablets)
EU/2/26/361/020 (900 mg lotilaner + 33.75 mg milbemycin oxime; 18 chewable tablets)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Lotilaner/Milbemycin Elanco

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

1.4-2.8 kg
> 2.8-5.5 kg
> 5.5-11 kg
> 11-22 kg
> 22-45 kg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Lotilaner/Milbemycin Elanco 56.25 mg/2.11 mg chewable tablets for dogs (1.4-2.8 kg)
Lotilaner/Milbemycin Elanco 112.5 mg/4.22 mg chewable tablets for dogs (> 2.8-5.5 kg)
Lotilaner/Milbemycin Elanco 225 mg/8.44 mg chewable tablets for dogs (> 5.5-11 kg)
Lotilaner/Milbemycin Elanco 450 mg/16.88 mg chewable tablets for dogs (> 11-22 kg)
Lotilaner/Milbemycin Elanco 900 mg/33.75 mg chewable tablets for dogs (> 22-45 kg)

2. Composition

Each chewable tablet contains:

Active substances:	**Lotilaner**	**Milbemycin oxime**
Dogs (1.4-2.8 kg)	56.25 mg	2.11 mg
Dogs (> 2.8-5.5 kg)	112.5 mg	4.22 mg
Dogs (> 5.5-11 kg)	225 mg	8.44 mg
Dogs (> 11-22 kg)	450 mg	16.88 mg
Dogs (> 22-45 kg)	900 mg	33.75 mg

White to beige round biconvex chewable tablet with brownish spots and bevelled edges with letter "I" debossed on one side of the tablet.

3. Target species

Dogs.

4. Indications for use

For use in dogs with, or at risk from, mixed infestations/infections by ticks, fleas, mites, gastrointestinal nematodes, heartworm and/or lungworm. This veterinary medicinal product is only indicated for use when treatment against ticks/fleas/mites and gastrointestinal nematodes or the treatment against ticks/fleas/mites and prevention of heartworm disease/angiostrongylosis is indicated at the same time.

Ectoparasites
For the treatment of tick (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus* and *I. hexagonus*) and flea (*Ctenocephalides felis* and *C. canis*) infestations in dogs.

This veterinary medicinal product provides immediate and persistent killing activity for 1 month for ticks and fleas.

The veterinary medicinal product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

For reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for one month. The effect is indirect due to the activity of the veterinary medicinal

product against the vector.

For the treatment of demodicosis (caused by *Demodex canis*).

For the treatment of sarcoptic mange (*Sarcoptes scabiei* var. *canis*).

Gastrointestinal Nematodes
Treatment of gastrointestinal nematodes: hookworm (L4, immature adult (L5) and adult *Ancylostoma caninum*), roundworms (L4, immature adult (L5) and adult *Toxocara canis*, and adult *Toxascaris leonina*) and whipworm (adult *Trichuris vulpis*).

Heartworm
Prevention of heartworm disease (*Dirofilaria immitis*).

Lungworm
Prevention of angiostrongylosis by reduction of the level of infection with immature adult (L5) and adult stages of *Angiostrongylus vasorum* (lungworm) with monthly administration.

5. Contraindications

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

6. Special warnings

Special warnings:
The possibility that other animals in the same household can be a source of re-infection with ticks, fleas, mites, gastrointestinal nematodes, heartworm and/or lungworm should be considered, and these should be treated as necessary with an appropriate product.

The product should be used in dogs with, or at risk from, mixed infestations of ectoparasites (ticks, fleas or mites) and endoparasites (gastrointestinal nematodes and/or for prevention of heartworm/lungworm). In the absence of risk of co-infestation by external and internal parasites, a narrow spectrum product should be used.

Ticks and fleas must attach to the host and commence feeding in order to be exposed to the active substance; therefore, the risk of the transmission of tick/flea-borne diseases cannot be excluded. Specifically, as an acaricidal effect against *D. reticulatus* may take up to 48 hours, transmission of *B. canis canis* during the first 48 hours cannot be excluded.

For the treatment of infections with gastrointestinal nematodes the need for, and the frequency of, re-treatment as well as the choice of the treatment (monosubstance or combination product) should be evaluated by the prescribing veterinarian.

Maintenance of the efficacy of macrocyclic lactones is critical for *Dirofilaria immitis* prevention, therefore, to minimise the risk of resistance selection, it is recommended that dogs should be checked for both circulating antigens and blood microfilariae at the beginning of each heartworm season prior to starting monthly preventive treatments. The product is not effective against adult *D. immitis* and is not indicated for microfilariae clearance.

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 infection/infestation based on its epidemiological features, for each individual animal.

Special precautions for safe use in the target species:

All safety and efficacy data have been acquired from dogs and puppies 8 weeks of age and older and 1.4 kg of bodyweight and greater. Use of this veterinary medicinal product in puppies younger than 8 weeks of age or less than 1.4 kg of bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

The recommended dose should be strictly observed in MDR1 mutant ($^{-/-}$) dogs with a non-functional P-glycoprotein, which may include Collies and related breeds.

Prior to first administration, dogs in heartworm endemic areas or who have visited heartworm endemic areas must be tested for existing heartworm infection. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to kill adult heartworms.

Administration of products containing milbemycin oxime (such as this product) to dogs with a high number of circulating microfilariae is not recommended in order to avoid hypersensitivity reactions associated with the release of proteins from dead or dying microfilariae.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Accidental ingestion may cause gastrointestinal disturbances. In order to prevent access by children, keep the chewable tablets in the blister packs until required and keep the blister packs in the outer carton out of the reach of children.

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

Wash hands after handling the tablets.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy or lactation. Laboratory studies in rats have not produced any evidence of teratogenic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

Fertility:
The safety of the veterinary medicinal product has not been established in breeding dogs.
Laboratory studies in rats have not produced any adverse effect on the reproductive capacity of males and females. Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Lotilaner and milbemycin oxime have been shown to be a substrate for P-glycoprotein (P-gp) and therefore could interact with other P-gp substrates (e.g. digoxin, doxorubicin) or other macrocyclic lactones. Therefore, concomitant treatment with other P-gp substrates could lead to enhanced toxicity.

Overdose:
No adverse reactions, other than those listed in section Adverse events, were observed in puppies (starting at 8-9 weeks of age) after administering up to 5 times the maximum recommended dose over 1-5 days (consecutive daily dosing) at monthly intervals on 9 occasions; or in adult dogs (starting at 11 months of age) after administering up to 5 times the maximum recommended dose over 1-5 days (consecutive daily dosing) at monthly intervals on 7 occasions; or in adult dogs (approximately 12 months old) after administration up to 6 times the maximum recommended dose as a bolus on a single occasion.

After administration of 5 times the maximum recommended dose to MDR1 mutant ($^{-/-}$) dogs with a non-functional P-glycoprotein, transient depression, ataxia, tremors, mydriasis and/or excessive salivation were observed.

7. Adverse events

Dogs:

Uncommon (1 to 10 animals / 1 000 animals treated):	Behavioural disorder [1,2] Diarrhoea[2], Vomiting[2] Muscle tremor[2] Pruritus (itching)[2] Anorexia (loss of appetite)[2], Lethargy[2]
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Ataxia (incoordination)[3], Convulsion[3], Muscle tremor[3]

[1] Changes in behaviour
[2] Generally self-limiting and of short duration.
[3] These signs typically resolve without treatment.

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 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

Oral use.

The veterinary medicinal product should be administered in accordance with the following table to ensure a dose of 20 to 41 mg lotilaner/kg bodyweight and 0.75 to 1.53 mg milbemycin oxime/kg bodyweight.

Dog bodyweight	**Strength and number of Lotilaner/Milbemycin Elanco chewable tablets to be administered**				
	56.25 mg/ 2.11 mg	112.5 mg/ 4.22 mg	225 mg/ 8.44 mg	450 mg/ 16.88 mg	900 mg/ 33.75 mg
1.4-2.8 kg	1				
> 2.8-5.5 kg		1			
> 5.5-11 kg			1		
> 11-22 kg				1	
> 22-45 kg					1
> 45 kg	Appropriate combination of tablets				

Use an appropriate combination of available strengths to achieve the recommended dose of 20–41 mg lotilaner/kg and 0.75–1.53 mg milbemycin oxime/kg for animals > 45 kg bodyweight. 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 infestations/infections with parasites, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle. If based on the veterinarian's opinion the dog requires re-administration(s) of the product, any subsequent administration(s) must follow the 1-month interval schedule.

Method of administration:
The veterinary medicinal product is a palatable chewable flavoured tablet. Administer the chewable tablet(s) with or after food.

9. Advice on correct administration

Dogs living in non-heartworm endemic areas:
The veterinary medicinal product can be used as part of the seasonal treatment of ticks and/or fleas in dogs with diagnosed, or at risk from, concurrent gastrointestinal nematode infections or at risk of lungworm. A single treatment is effective for the treatment of gastrointestinal nematodes.

Dogs living in heartworm endemic areas:
Prior to treatment with the veterinary medicinal product the advice in section Special warnings should be considered.

For the prevention of heartworm disease and the concurrent treatment of tick and/or flea infestations, the veterinary medicinal product must be given at regular monthly intervals during the time of the year when mosquitoes, ticks and/or fleas are present. The first dose of the veterinary medicinal product may be given after first possible exposure to mosquitoes, but not more than one month after this exposure.

When the veterinary medicinal product is used to replace another heartworm preventive product, the first dose of the product must be given within a month of the last dose of the former medication. Dogs travelling to a heartworm region should start medication within a month after arrival there. Heartworm prevention treatment should be continued monthly, with the last administration being given 1 month after the dog has left the region.

Lungworm:
In endemic areas, monthly administration of the veterinary medicinal product will reduce the level of infection with immature adults (L5) and adults of *Angiostrongylus vasorum* in the heart and lungs. It is recommended that lungworm prevention should be continued until at least 1 month after the last exposure to slugs and snails.

Seek veterinary advice regarding information on the optimal time to start treatment with this veterinary medicinal product.

For the treatment of demodicosis (caused by *Demodex canis*):
Monthly administration of the product for two consecutive months is efficacious and leads to a marked improvement of clinical signs. Treatment should be continued until two negative skin scrapings are obtained one month apart. Severe cases may require prolonged monthly treatments. As demodicosis is a multi-factorial disease, where possible, it is advisable to also treat any underlying disease appropriately.

For the treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*):
Monthly administration of the product for two consecutive months. Further monthly administration of the product may be required based on clinical assessment and skin scrapings.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Store in the original package.

This veterinary medicinal product does not require any special storage conditions.

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

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.

14. Marketing authorisation numbers and pack sizes

EU/2/26/361/001-020

Aluminium/aluminium blisters packaged into an outer cardboard box.
Pack sizes of 1, 3, 6 or 18 tablets.

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:
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