ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Credelio 56 mg chewable tablets for dogs (1.3–2.5 kg)
Credelio 112 mg chewable tablets for dogs (>2.5–5.5 kg)
Credelio 225 mg chewable tablets for dogs (>5.5–11 kg)
Credelio 450 mg chewable tablets for dogs (>11–22 kg)
Credelio 900 mg chewable tablets for dogs (>22–45 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each chewable tablet contains:

Credelio chewable tablets	lotilaner (mg)
for dogs (1.3–2.5 kg)	56.25
for dogs (>2.5–5.5 kg)	112.5
for dogs (>5.5–11 kg)	225
for dogs (>11–22 kg)	450
for dogs (>22–45 kg)	900

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablet.
White to beige round chewable tablets with brownish spots.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For the treatment of flea and tick infestations in dogs.

This veterinary medicinal product provides immediate and persistent killing activity for 1 month for fleas (*Ctenocephalides felis* and *C. canis*) and ticks (*Rhipicephalus sanguineus, Ixodes ricinus, I. hexagonus and Dermacentor reticulatus*).

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.

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

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

Parasites need to start feeding on the host to become exposed to lotilaner; therefore the risk of the transmission of parasite borne diseases cannot be completely excluded.

4.5 Special precautions for use

Special precautions for use in animals

All safety and efficacy data have been acquired from dogs and puppies 8 weeks of age and older and 1.3 kg of body weight and greater. Use of this veterinary medicinal product in puppies younger than 8 weeks of age or less than 1.3 kg of body weight should be based on a benefit-risk assessment by the responsible veterinarian.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

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

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

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

4.8 Interaction with other medicinal products and other forms of interaction

None known. During clinical testing, no interactions between Credelio chewable tablets and routinely used veterinary medicinal products were observed.

4.9 Amounts to be administered and administration route

For oral use.

The veterinary medicinal product should be administered in accordance with the following table to ensure a dose of 20 to 43 mg lotilaner/kg bodyweight.

Body weight of dog (kg)	**Strength and number of tablets to be administered**				
	Credelio 56 mg	Credelio 112 mg	Credelio 225 mg	Credelio 450 mg	Credelio 900 mg
1.3–2.5	1				
>2.5–5.5		1			
>5.5–11.0			1		
>11.0–22.0				1	
>22.0–45.0					1
>45	Appropriate combination of tablets				

Use an appropriate combination of available strengths to achieve the recommended dose of 20–43 mg/kg.

Credelio is a palatable chewable flavoured tablet. Administer the chewable tablet(s) monthly with or after food.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No adverse reactions were observed following oral administration to puppies aged 8–9 weeks and weighing 1.3–3.6 kg treated with overdoses of up to 5 times the maximum recommended dose (43 mg, 129 mg and 215 mg lotilaner/kg bodyweight) on eight occasions at monthly intervals.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: ectoparasiticides for systemic use, isoxazolines.
ATCvet code: QP53BE04

5.1 Pharmacodynamic properties

Lotilaner, a pure enantiomer from the isoxazoline class is active against fleas (*Ctenocephalides felis* and *Ctenocephalides canis*) as well as the tick species *Dermacentor reticulatus, Ixodes hexagonus, Ixodes ricinus and Rhipicephalus sanguineus*.

Lotilaner is a potent inhibitor of gamma–aminobutyric acid (GABA)-gated chloride channels, resulting in rapid death of ticks and fleas. The activity of lotilaner was not 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 fleas, the onset of efficacy is within 4 hours of attachment for one month after product administration. Fleas on the animal prior to administration are killed within 6 hours.
For ticks, the onset of efficacy is within 48 hours of attachment for one month after product administration. Existing *I. ricinus* ticks on the animal prior to administration are killed within 8 hours.

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

5.2 Pharmacokinetic particulars

Following oral administration, lotilaner is readily absorbed and peak blood concentration is reached within 2 hours. Food enhances the absorption. The terminal half-life is approximately 4 weeks. This long terminal half-life provides effective blood concentrations for the entire duration of the inter-dosing interval.
The major route of elimination is biliary excretion and renal excretion is the minor route of elimination (less than 10% of the dose). Lotilaner is metabolized to a small extent into more hydrophilic compounds which are observed in faeces and urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, powdered
Lactose monohydrate
Silicified microcrystalline cellulose
Meat dry flavour
Crospovidone
Povidone K30
Sodium laurilsulfate
Silica, colloidal anhydrous
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

6.4. Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

The tablets are packaged in aluminium/aluminium blisters packaged into an outer cardboard box.
Each tablet strength is available in pack sizes of 1, 3 or 6 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Elanco Europe Ltd
Lilly House, Priestley Road
Basingstoke
Hampshire
RG24 9NL
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/17/206/001–015

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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

10 DATE OF REVISION OF THE TEXT

<{DD/MM/YYYY}>

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Elanco France S.A.S
26 Rue de la Chapelle
68330 Huningue
FRANCE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Credelio 56 mg chewable tablets for dogs (1.3–2.5 kg)
Credelio 112 mg chewable tablets for dogs (>2.5–5.5 kg)
Credelio 225 mg chewable tablets for dogs (>5.5–11 kg)
Credelio 450 mg chewable tablets for dogs (>11–22 kg)
Credelio 900 mg chewable tablets for dogs (>22–45 kg)

lotilaner

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

56 mg lotilaner
112 mg lotilaner
225 mg lotilaner
450 mg lotilaner
900 mg lotilaner

3. PHARMACEUTICAL FORM

Chewable tablet

4. PACKAGE SIZE

1 tablet
3 tablets
6 tablets

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Administer with or after food.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Elanco Europe Ltd
Lilly House, Priestley Road
Basingstoke
Hampshire
RG24 9NL
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/17/206/001 (56 mg lotilaner; 1 chewable tablet)
EU/2/17/206/002 (56 mg lotilaner; 3 chewable tablets)
EU/2/17/206/003 (56 mg lotilaner; 6 chewable tablets)
EU/2/17/206/004 (112 mg lotilaner; 1 chewable tablet)
EU/2/17/206/005 (112 mg lotilaner; 3 chewable tablets)
EU/2/17/206/006 (112 mg lotilaner; 6 chewable tablets)
EU/2/17/206/007 (225 mg lotilaner; 1 chewable tablet)

EU/2/17/206/008 (225 mg lotilaner; 3 chewable tablets)
EU/2/17/206/009 (225 mg lotilaner; 6 chewable tablets)
EU/2/17/206/010 (450 mg lotilaner; 1 chewable tablet)
EU/2/17/206/011 (450 mg lotilaner; 3 chewable tablets)
EU/2/17/206/012 (450 mg lotilaner; 6 chewable tablets)
EU/2/17/206/013 (900 mg lotilaner; 1 chewable tablet)
EU/2/17/206/014 (900 mg lotilaner; 3 chewable tablets)
EU/2/17/206/015 (900 mg lotilaner; 6 chewable tablets)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Credelio 56 mg
Credelio 112 mg
Credelio 225 mg
Credelio 450 mg
Credelio 900 mg

lotilaner (EN or Latin)

1.3–2.5 kg
>2.5–5.5 kg
>5.5–11 kg
>11–22 kg
>22–45 kg

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Credelio 56 mg chewable tablets for dogs (1.3–2.5 kg)
Credelio 112 mg chewable tablets for dogs (>2.5–5.5 kg)
Credelio 225 mg chewable tablets for dogs (>5.5–11 kg)
Credelio 450 mg chewable tablets for dogs (>11–22 kg)
Credelio 900 mg chewable tablets for dogs (>22–45 kg)

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Elanco Europe Ltd., Lilly House, Priestley Road, Basingstoke, Hampshire, RG24 9NL, United Kingdom

Manufacturer responsible for batch release:
Elanco France S.A.S., 26 rue de la Chapelle, 68330 Huningue, France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Credelio 56 mg chewable tablets for dogs (1.3–2.5 kg)
Credelio 112 mg chewable tablets for dogs (>2.5–5.5 kg)
Credelio 225 mg chewable tablets for dogs (>5.5–11 kg)
Credelio 450 mg chewable tablets for dogs (>11–22 kg)
Credelio 900 mg chewable tablets for dogs (>22–45 kg)

lotilaner

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each chewable tablet contains:

Credelio chewable tablets	**lotilaner (mg)**
for dogs (1.3–2.5 kg)	56.25
for dogs (>2.5–5.5 kg)	112.5
for dogs (>5.5–11 kg)	225
for dogs (>11–22 kg)	450
for dogs (>22–45 kg)	900

White to beige round chewable tablets with brownish spots.

4. INDICATION(S)

Treatment of flea and tick infestations in dogs.

This veterinary medicinal product provides immediate and persistent killing activity for 1 month for fleas (*Ctenocephalides felis* and *C. canis*) and ticks (*Rhipicephalus sanguineus, Ixodes ricinus, I. hexagonus, and Dermacentor reticulatus*).

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.

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

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

None known.

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs.

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

For oral use.

The veterinary medicinal product should be administered in accordance with the following table to ensure a dose of 20 to 43 mg lotilaner/kg bodyweight.

Body weight of dog (kg)	**Strength and number of tablets to be administered**				
	Credelio 56 mg	Credelio 112 mg	Credelio 225 mg	Credelio 450 mg	Credelio 900 mg
1.3–2.5	1				
>2.5–5.5		1			
>5.5–11			1		
>11–22				1	
>22–45					1
>45	Appropriate combination of tablets				

Use an appropriate combination of available strengths to achieve the recommended dose of 20–43 mg/kg.

9. ADVICE ON CORRECT ADMINISTRATION

Credelio is a palatable chewable flavoured tablet. Administer the chewable tablet(s) monthly with or after food.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
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 box and blister after EXP. The expiry date refers to the last day of that month.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Parasites need to start feeding on the host to become exposed to lotilaner; therefore the risk of the transmission of parasite borne diseases cannot be completely excluded.

Special precautions for use in animals:
All safety and efficacy data have been acquired from dogs and puppies 8 weeks of age and older and 1.3 kg of body weight and greater. The administration of this product in puppies younger than 8 weeks of age or less than 1.3 kg of body weight should be based on a benefit-risk assessment by the responsible veterinarian.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after handling the product.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or label to the physician.

Pregnancy and lactation:
Laboratory studies in rats have not produced any evidence of teratogenic effects.
The safety of the veterinary medicinal product in pregnant and lactating dogs has not been established. Use only accordingly to the benefit/risk assessment of the responsible veterinarian.

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

Interaction with other medicinal products and other forms of interaction:
None known. During clinical testing, no interactions between Credelio chewable tablets and routinely used veterinary medicinal products were observed.

Overdose (symptoms, emergency procedures, antidotes):
No adverse reactions were observed following oral administration to puppies aged 8–9 weeks and weighing 1.3–3.6 kg treated with overdoses of up to 5 times the maximum recommended dose (43 mg, 129 mg and 215 mg lotilaner/kg bodyweight) on eight occasions at monthly intervals.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

15. OTHER INFORMATION

Lotilaner, a pure enantiomer from the isoxazoline class is active against fleas (*Ctenocephalides felis* and *Ctenocephalides canis*) as well as the tick species *Dermacentor reticulatus, Ixodes hexagonus, Ixodes ricinus and Rhipicephalus sanguineus*.

Lotilaner is a potent inhibitor of gamma–aminobutyric acid (GABA)-gated chloride channels, resulting in rapid death of ticks and fleas. The activity of lotilaner was not 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 fleas, the onset of efficacy is within 4 hours of attachment for one month after product administration. Fleas on the animal prior to administration are killed within 6 hours.

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

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

Each strength of Credelio chewable tablets is available in pack sizes of 1, 3 or 6 tablets.
Not all pack sizes may be marketed.