ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BRAVECTO CombiUNO 25 mg/1.875 mg chewable tablets for dogs (1.27–2.5 kg)
BRAVECTO CombiUNO 50 mg/3.75 mg chewable tablets for dogs (> 2.5–5 kg)
BRAVECTO CombiUNO 100 mg/7.5 mg chewable tablets for dogs (> 5–10 kg)
BRAVECTO CombiUNO 200 mg/15 mg chewable tablets for dogs (> 10–20 kg)
BRAVECTO CombiUNO 400 mg/30 mg chewable tablets for dogs (> 20–40 kg)
BRAVECTO CombiUNO 600 mg/45 mg chewable tablets for dogs (> 40–60 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Active substances:

BRAVECTO CombiUNO chewable tablets for dogs	Fluralaner (mg)	Milbemycin oxime (mg)
1.27–2.5 kg	25	1.875
> 2.5–5 kg	50	3.75
> 5–10 kg	100	7.5
> 10–20 kg	200	15
> 20–40 kg	400	30
> 40–60 kg	600	45

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Natural beef flavour	
Sucrose	
Maize starch	
Sodium laurilsulfate	
Disodium pamoate monohydrate	
Sodium starch glycolate (type A)	
Aspartame	
Butylhydroxytoluene (E 321)	0.75 mg (1.27–2.5 kg) 1.5 mg (> 2.5–5 kg) 3 mg (> 5–10 kg) 6 mg (> 10 – 20 kg) 12 mg (> 20–40 kg) 18 mg (> 40–60 kg)
Citric acid monohydrate	
Glycerol	
Triglycerides, medium-chain	
Macrogol 3350	

Light brown to dark brown chewable tablet. Some marbling or specks (or both) may be visible.

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 parasitic infestations by ticks or fleas, gastrointestinal nematodes, lungworm and/or heartworm. The veterinary medicinal product is exclusively indicated when use against ticks or fleas and gastrointestinal nematodes is indicated at the same time. The veterinary medicinal product also provides concurrent efficacy for the prevention of heartworm disease and angiostrongylosis.

For the treatment of tick and flea infestations on dogs providing immediate and persistent flea (*Ctenocephalides felis* and *C. canis*) killing activity and immediate and persistent tick (*Dermacentor reticulatus, Ixodes hexagonus, I. ricinus,* and *Rhipicephalus sanguineus)* killing activity for 1 month.

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 *D. reticulatus* for 1 month. The effect is indirect due to the product's activity against the vector.

For reduction of the risk of infection with *Dipylidium caninum via* transmission by *C. felis* for 1 month. The effect is indirect due to the product's activity against the vector.

Treatment of infections with gastrointestinal nematodes of the following species: roundworms (immature adult (L5) and adult stages of *Toxocara canis,* and adult stages of *Toxascaris leonina*), hookworms (immature adult (L5) and adult stages of *Ancylostoma caninum*) and whipworm (adult stage of *Trichuris vulpis*).

Prevention of heartworm disease (*Dirofilaria immitis*).

Prevention of angiostrongylosis (by reduction of the level of infection with immature adult (L5) and adult stages of *Angiostrongylus vasorum*) 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

Parasites need to start feeding on the host to become exposed to fluralaner; therefore, the risk of the transmission of parasite borne diseases (including *B. canis canis* and *D. caninum*) cannot be completely excluded.

Dogs in areas endemic for heartworm (or those which have travelled to endemic areas) may be infected with adult heartworms. No therapeutic effect against adult *Dirofilaria immitis* has been established. It is therefore recommended, in accordance with good veterinary practice, that all animals 6 months of age or more, living, or have travelled to, in areas where a vector exists, should be tested for existing adult heartworm infections before beginning preventive use with the veterinary medicinal product.

For the treatment of infections with the 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.

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 veterinary medicinal 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 the absence of risk of co-infection with ecto-and endoparasites, a narrow spectrum product should be used.

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

3.5 Special precautions for use

Special precautions for safe use in the target species:
Use with caution in dogs with pre-existing epilepsy.

In the absence of available data, treatment of puppies less than 8 weeks of age and/or dogs less than 1.27 kg bodyweight (BW) should be based on a benefit-risk assessment by the responsible veterinarian.

In (MDR1-/-) dogs, safety of the veterinary medicinal product has been investigated after multiple monthly administrations in a laboratory study. The recommended dose should be strictly observed in MDR1 mutant (-/-) dogs with a non-functional P-glycoprotein, which may include, but not necessarily be limited to, Collies and related breeds. Please see also section 3.10 'Symptoms of overdose (and where applicable, emergency procedures and antidotes)'.

The veterinary medicinal product should not be administered at intervals shorter than 1 month as the safety at shorter intervals has not been tested.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to any of the active substances and/or excipients should avoid contact with the veterinary medicinal product.

This veterinary medicinal product is harmful after ingestion. Keep in the original packaging until use, in order to prevent children from getting direct access to the veterinary medicinal product. In case of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician.

Do not eat, drink or smoke while handling the veterinary medicinal product.

This veterinary medicinal product may irritate the eyes. Avoid contact with eyes. If in eyes, wash out immediately with water.

Wash hands thoroughly with soap and water immediately after use of the veterinary medicinal product.

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

3.6 Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Emesis[1]
Uncommon (1 to 10 animals / 1 000 animals treated):	Diarrhea[1], Hypersalivation[1], Retching[1]; Lethargy[2], Decreased appetite[2]
Rare (1 to 10 animals / 10 000 animals treated):	Blood in faeces[1]
Very rare (< 1 animal / 10 000 animals treated, including isolated reports):	Muscle tremor, Ataxia, Convulsion[3]

[1] usually resolves within 1 day
[2] usually resolves within 2 days
[3] may be serious

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 and lactation or in dogs intended for breeding.

Pregnancy and lactation:
The use is not recommended during pregnancy and lactation.

Fertility:
The use is not recommended in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

Macrocyclic lactones including milbemycin oxime have been shown to be P-glycoprotein substrates. Therefore, during treatment with the veterinary medicinal product, other products that are substrates or inhibitors of P-glycoprotein (e.g., cyclosporine, digoxin, doxorubicin, ketoconazole, spinosad) should only be used concomitantly according to the benefit/risk assessment of the responsible veterinarian.

Fluralaner is highly bound to plasma proteins and might compete with other highly bound active substances such as non-steroidal anti-inflammatory drugs (NSAIDs) and the coumarin derivative warfarin. Incubation of fluralaner in the presence of carprofen or warfarin in dog plasma at maximum expected plasma concentrations did not reduce the protein binding of fluralaner, carprofen or warfarin.

During clinical field testing, no interactions between the veterinary medicinal product and routinely used veterinary medicinal products were observed.

3.9 Administration routes and dosage

For oral use.

Dose:

The veterinary medicinal product should be administered at a dose of 10–20 mg/kg of fluralaner and 0.75–1.5 mg/kg of milbemycin oxime in accordance with the following table:

Bodyweight (kg) of dog	**Number and strength of BRAVECTO CombiUNO chewable tablet to be administered**					
	25 mg/ 1.875 mg	50 mg/ 3.75 mg	100 mg/ 7.5 mg	200 mg/ 15 mg	400 mg/ 30 mg	600 mg/ 45 mg
1.27–2.5	1					
> 2.5–5		1				
> 5–10			1			
> 10–20				1		
> 20–40					1	
> 40–60						1

The chewable tablet should not be broken or divided.
For dogs above 60 kg, appropriate combinations of chewable tablets should be used.
To ensure a correct dosage, bodyweight should be determined as accurately as possible.
Underdosing could result in ineffective use and may favour resistance development.

Method of administration:
Administer the veterinary medicinal product at or around the time of feeding.

The veterinary medicinal product is a flavoured chewable tablet. Tablets can be offered to the dog, given with food or placed directly into the mouth. The dog should be observed during administration to confirm that the full chewable tablet is swallowed.

Treatment schedule:
For infestations with ticks, fleas, gastrointestinal nematodes, heartworm and lungworm, the need for and frequency of re-treatments should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Ticks and fleas:
For optimal treatment and control of flea and tick infestation, the veterinary medicinal product should be administered at intervals of 1 month.

Gastrointestinal nematodes:
For the concurrent treatment of infections with gastrointestinal nematodes, a single dose of the product should be administered. Where necessary, dogs can be re-treated at 1-month intervals.

Heartworm:
The veterinary medicinal product kills *Dirofilaria immitis* larvae up to one month after their transmission. Therefore, the veterinary medicinal product should be administered at regular monthly intervals during the time of the year when vectors (mosquitoes) are present. Administration should start in the month after the first expected exposure to the vectors and should continue until 1-month after the last exposure to the vectors.

Dogs in areas endemic for heartworm, or dogs which have travelled to endemic areas, may be infected with adult heartworms. Therefore prior to administration of the veterinary medicinal product for the concurrent prevention of infection with adult *D. immitis*, the advice provided in section 3.4 should be considered.

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 4 months 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.

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

No adverse reactions were observed following oral administration to puppies aged 56 to 58 days and weighing 1.4 to 1.8 kg treated with overdoses of up to 5 times the maximum recommended dose (20 mg fluralaner + 1.5 mg milbemycin oxime, 60 mg fluralaner + 4.5 mg milbemycin oxime and 100 mg fluralaner + 7.5 mg milbemycin oxime/kg BW) on 7 occasions.

In a laboratory study the veterinary medicinal product was administered on 3 occasions monthly at 1-, 3- and 5-times the maximum recommended dose to dogs with a deficient multidrug-resistance protein 1 (MDR1-/-). After repeated administration of 3- and 5-times the maximum recommended dose, mostly within 24 hours, ataxia and emesis were observed. Overall, the veterinary medicinal product was tolerated in MDR1-/- dogs following oral administration.

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

Fluralaner:
Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Dermacentor reticulatus*, *Ixodes hexagonus, I. ricinus and Rhipicephalus sanguineus*) and fleas (*Ctenocephalides canis* and *C. felis*) on the dog.

The onset of effect is within 12 hours for fleas (*C. felis*) and 24 hours of attachment for *R. sanguineus* and 24 hours for *D. reticulatus* ticks.

Fluralaner reduces the risk of infection with *Babesia canis canis* via transmission by *D. reticulatus* by killing the ticks before disease transmission occurs.

Fluralaner reduces the risk of infection with *Dipylidium caninum* via transmission by *C. felis* by killing the fleas before disease transmission occurs.

Fluralaner has a high potency against ticks and fleas by exposure via feeding, i.e., it is systemically active on target parasites.

Fluralaner is a potent inhibitor of parts of the arthropod nervous system by acting antagonistically on ligand-gated chloride channels (GABA-receptor and glutamate-receptor).

In molecular on-target studies on insect GABA receptors of fleas and flies, fluralaner is not affected by dieldrin resistance.

In *in vitro* bioassays, fluralaner is not affected by proven field resistances against amidines (tick), organophosphates (tick, mite), cyclodienes (tick, flea, fly), macrocyclic lactones (sea lice), phenylpyrazoles (tick, flea), benzophenyl ureas (tick), pyrethroids (tick, mite), and carbamates (tick, mite).

Newly emerged fleas on a dog are killed before viable eggs are produced. An *in vitro* study demonstrated that very low concentrations of fluralaner also stop the production of viable eggs by fleas. The monthly use of the product breaks the flea lifecycle, and new infestations are prevented due to the rapid onset of action and lasting efficacy against adult fleas on the animal and the absence of viable egg production. The product contributes towards the control of the environmental flea populations in areas to which treated dogs have access.

Milbemycin oxime:
Milbemycin oxime is a systemically active macrocyclic lactone originally isolated from the fermentation of *Streptomyces hygroscopius aureolacrimosus* and recently from *Streptomyces bingchenggensis* containing two major factors, A3 and A4.

Milbemycin oxime is an antiparasitic endectocide acting on invertebrate neurotransmission by hyperpolarization of the neuromuscular membrane. It increases nematode and insect membrane permeability to chloride ions via glutamate-gated chloride ion channels. This leads to flaccid paralysis and death of the parasite.

Milbemycin oxime is active against mites, larval and adult stages of nematodes (*A. caninum, T. canis, T. vulpis,* and *T. leonina*), as well as larvae (L3/L4) of *Dirofilaria immitis*, and immature adults (L5) of *Angiostrongylus vasorum*.

4.3 Pharmacokinetics

After oral administration, fluralaner and milbemycin oxime are readily absorbed, reaching individual maximum plasma concentrations between ~1 and 7 days or between 1 and 6 hours post administration, respectively. Fluralaner is quantifiable until the last sampling timepoint, 71 days post dosing, i.e., fluralaner declines slowly from canine plasma, whereas milbemycin oxime declines readily from dog plasma and is quantifiable until 8 to 16 days post administration. Oral bioavailability of fluralaner is between 47.4 and 55.1%, whereas milbemycin oxime bioavailability is slightly higher between 66.5 and 75.6%. Fluralaner and milbemycin oxime show a relatively high volume of distribution (1.4 to 2.0 ml/kg BW for fluralaner, 20 to 31 and 3.4 to 5.1 ml/kg BW, for milbemycin oxime A3 and A4, respectively), a low systemic clearance accompanied with a long elimination half-life for fluralaner (around 11 days) and a relatively long elimination half-life for milbemycin oxime (around 19 hours for A3 and 37 hours for A4) at the dose range in clinical use, thus demonstrating persistent effects in the dog during the intended treatment intervals. Fluralaner and milbemycin oxime are mainly excreted via faeces.
For fluralaner, accumulation has been observed after repeated monthly dosing. See section 3.10.

The pharmacokinetic profiles of fluralaner and milbemycin oxime are not affected by co-administration.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

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

5.3 Special precautions for storage

Do not store above 30 °C.

5.4 Nature and composition of immediate packaging

PVC-oPA-aluminium-oPA-PVC foil blister sealed with PET-aluminium foil lid.

Each blister strip contains one chewable tablet.

Pack sizes:
Cardboard box containing 1 blister strip with 1 chewable tablet
Cardboard box containing 3 blister strips with 1 chewable tablet each
Cardboard box containing 6 blister strips with 1 chewable tablet each

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 fluralaner and milbemycin oxime 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

Intervet International B.V.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/25/350/001–018

8. DATE OF FIRST AUTHORISATION

30/07/2025.

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

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

BRAVECTO CombiUNO 25 mg/1.875 mg chewable tablets for dogs (1.27–2.5 kg)
BRAVECTO CombiUNO 50 mg/3.75 mg chewable tablets for dogs (> 2.5–5 kg)
BRAVECTO CombiUNO 100 mg/7.5 mg chewable tablets for dogs (> 5–10 kg)
BRAVECTO CombiUNO 200 mg/15 mg chewable tablets for dogs (> 10–20 kg)
BRAVECTO CombiUNO 400 mg/30 mg chewable tablets for dogs (> 20–40 kg)
BRAVECTO CombiUNO 600 mg/45 mg chewable tablets for dogs (> 40–60 kg)

2. STATEMENT OF ACTIVE SUBSTANCES

Each chewable tablet contains:

25 mg fluralaner/1.875 mg milbemycin oxime
50 mg fluralaner/3.75 mg milbemycin oxime
100 mg fluralaner/7.5 mg milbemycin oxime
200 mg fluralaner/15 mg milbemycin oxime
400 mg fluralaner/30 mg milbemycin oxime
600 mg fluralaner/45 mg milbemycin oxime

3. PACKAGE SIZE

1 chewable tablet
3 chewable tablets
6 chewable tablets

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.

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

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/25/350/001 (25 mg fluralaner/1.875 mg milbemycin oxime - 1 tablet)
EU/2/25/350/002 (25 mg fluralaner/1.875 mg milbemycin oxime - 3 tablets)
EU/2/25/350/003 (25 mg fluralaner/1.875 mg milbemycin oxime - 6 tablets)
EU/2/25/350/004 (50 mg fluralaner/3.75 mg milbemycin oxime - 1 tablet)
EU/2/25/350/005 (50 mg fluralaner/3.75 mg milbemycin oxime - 3 tablets)
EU/2/25/350/006 (50 mg fluralaner/3.75 mg milbemycin oxime - 6 tablets)
EU/2/25/350/007 (100 mg fluralaner/7.5 mg milbemycin oxime - 1 tablet)
EU/2/25/350/008 (100 mg fluralaner/7.5 mg milbemycin oxime - 3 tablets)
EU/2/25/350/009 (100 mg fluralaner/7.5 mg milbemycin oxime - 6 tablets)
EU/2/25/350/010 (200 mg fluralaner/15 mg milbemycin oxime - 1 tablet)
EU/2/25/350/011 (200 mg fluralaner/15 mg milbemycin oxime - 3 tablets)
EU/2/25/350/012 (200 mg fluralaner/15 mg milbemycin oxime - 6 tablets)
EU/2/25/350/013 (400 mg fluralaner/30 mg milbemycin oxime - 1 tablet)
EU/2/25/350/014 (400 mg fluralaner/30 mg milbemycin oxime - 3 tablets)
EU/2/25/350/015 (400 mg fluralaner/30 mg milbemycin oxime - 6 tablets)
EU/2/25/350/016 (600 mg fluralaner/45 mg milbemycin oxime - 1 tablet)
EU/2/25/350/017 (600 mg fluralaner/45 mg milbemycin oxime - 3 tablets)
EU/2/25/350/018 (600 mg fluralaner/45 mg milbemycin oxime - 6 tablets)

15. BATCH NUMBER

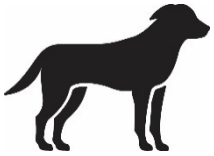
Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BRAVECTO CombiUNO



2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

25 mg/1.875 mg (1.27–2.5 kg)
50 mg/3.75 mg (> 2.5–5 kg)
100 mg/7.5 mg (> 5–10 kg)
200 mg/15 mg (> 10–20 kg)
400 mg/30 mg (> 20–40 kg)
600 mg/45 mg (> 40–60 kg)

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

BRAVECTO CombiUNO 25 mg/1.875 mg chewable tablets for dogs (1.27–2.5 kg)
BRAVECTO CombiUNO 50 mg/3.75 mg chewable tablets for dogs (> 2.5–5 kg)
BRAVECTO CombiUNO 100 mg/7.5 mg chewable tablets for dogs (> 5–10 kg)
BRAVECTO CombiUNO 200 mg/15 mg chewable tablets for dogs (> 10–20 kg)
BRAVECTO CombiUNO 400 mg/30 mg chewable tablets for dogs (> 20–40 kg)
BRAVECTO CombiUNO 600 mg/45 mg chewable tablets for dogs (> 40–60 kg)

2. Composition

Each chewable tablet contains:

Active substances:

BRAVECTO CombiUNO chewable tablets for dogs	Fluralaner (mg)	Milbemycin oxime (mg)
1.27–2.5 kg	25	1.875
> 2.5–5 kg	50	3.75
> 5–10 kg	100	7.5
> 10–20 kg	200	15
> 20–40 kg	400	30
> 40–60 kg	600	45

Excipients:

BRAVECTO CombiUNO chewable tablets for dogs	Butylhydroxytoluene (E 321) (mg)
1.27–2.5 kg	0.75
> 2.5–5 kg	1.5
> 5–10 kg	3
> 10–20 kg	6
> 20–40 kg	12
> 40–60 kg	18

Light brown to dark brown chewable tablet. Some marbling or specks (or both) may be visible.

3. Target species

Dogs. 

4. Indications for use

For dogs with, or at risk from, mixed parasitic infestations by ticks or fleas, gastrointestinal nematodes, lungworm and/or heartworm. The veterinary medicinal product is exclusively indicated when use against ticks or fleas and gastro-intestinal nematodes is indicated at the same time. The

veterinary medicinal product also provides concurrent efficacy for the prevention of heartworm disease and angiostrongylosis.

For the treatment of tick and flea infestations on dogs providing immediate and persistent flea (*Ctenocephalides felis* and *C. canis*) killing activity and immediate and persistent tick (*Dermacentor reticulatus, Ixodes hexagonus, I. ricinus,* and *Rhipicephalus sanguineus)* killing activity for 1 month.

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 *D. reticulatus* for 1 month. The effect is indirect due to the product's activity against the vector.

For reduction of the risk of infection with *Dipylidium caninum* via transmission by *C. felis* for 1 month. The effect is indirect due to the product's activity against the vector.

Treatment of infections with gastrointestinal nematodes of the following species: roundworms (immature adult (L5) and adult stages of *Toxocara canis,* and adult stage of *Toxascaris leonina*), hookworms (immature adult (L5) and adult stages of *Ancylostoma caninum*) and whipworm (adult stage of *Trichuris vulpis*).

Prevention of heartworm disease (*Dirofilaria immitis*).

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

5. Contraindications

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

6. Special warnings

Special warnings:
Parasites need to start feeding on the host to become exposed to fluralaner; therefore, the risk of the transmission of parasite borne diseases (including *B. canis canis* and *D. caninum*) cannot be completely excluded.
Dogs in areas endemic for heartworm (or those which have travelled to endemic areas) may be infected with adult heartworms. No therapeutic effect against adult *Dirofilaria immitis* has been established. It is therefore recommended, in accordance with good veterinary practice, that all animals 6 months of age or more, living, or have travelled to, in areas where a vector exists, should be tested for existing adult heartworm infections before beginning preventive use with the veterinary medicinal product.
For the treatment of infections with the 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.
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 veterinary medicinal 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 the absence of risk of co-infection with ecto-and endoparasites, a narrow spectrum product should be used.
The possibility that other animals in the same household can be a source of re-infection with ticks, fleas or gastrointestinal nematodes should be considered, and these should be treated as necessary with an appropriate product.

Special precautions for safe use in the target species:
Use with caution in dogs with pre-existing epilepsy.
In the absence of available data, treatment of puppies less than 8 weeks of age and/or dogs less than 1.27 kg bodyweight (BW) should be based on a benefit-risk assessment by the responsible veterinarian.
In (MDR1-/-) dogs, safety of the veterinary medicinal product has been investigated after multiple monthly administrations in a laboratory study. The recommended dose should be strictly observed in MDR1 mutant (-/-) dogs with a non-functional P-glycoprotein, which may include, but not necessarily be limited to, Collies and related breeds. Please see also section 6 'Overdose'.
The veterinary medicinal product should not be administered at intervals shorter than 1 month as the safety at shorter intervals has not been tested.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to any of the active substances and/or excipients should avoid contact with the veterinary medicinal product.
This veterinary medicinal product is harmful after ingestion.
Keep in the original packaging until use, in order to prevent children from getting direct access to the veterinary medicinal product. In case of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician.
Do not eat, drink or smoke while handling the veterinary medicinal product.
This veterinary medicinal product may irritate the eyes. Avoid contact with eyes. If in eyes, wash out immediately with water. Wash hands thoroughly with soap and water immediately after use of the veterinary medicinal product.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation or in dogs intended for breeding.
The use is not recommended during pregnancy and lactation.

Fertility:
The use is not recommended in breeding animals.

Interaction with other medicinal products and other forms of interaction:
Macrocyclic lactones including milbemycin oxime have been shown to be P-glycoprotein substrates. Therefore, during treatment with the veterinary medicinal product, other products that are substrates or inhibitors of P-glycoprotein (e.g., cyclosporine, digoxin, doxorubicin, ketoconazole, spinosad) should only be used concomitantly according to the benefit/risk assessment of the responsible veterinarian.
Fluralaner is highly bound to plasma proteins and might compete with other highly bound active substances such as non-steroidal anti-inflammatory drugs (NSAIDs) and the coumarin derivative warfarin. Incubation of fluralaner in the presence of carprofen or warfarin in dog plasma at maximum expected plasma concentrations did not reduce the protein binding of fluralaner, carprofen or warfarin. During clinical field testing, no interactions between the veterinary medicinal product and routinely used veterinary medicinal products were observed.

Overdose:
No adverse reactions were observed following oral administration to puppies aged 56 to 58 days and weighing 1.4 to 1.8 kg treated with overdoses of up to 5 times the maximum recommended dose (20 mg fluralaner + 1.5 mg milbemycin oxime, 60 mg fluralaner + 4.5 mg milbemycin oxime and 100 mg fluralaner + 7.5 mg milbemycin oxime/kg BW) on 7 occasions.
In a laboratory study the veterinary medicinal product was administered on 3 occasions monthly at 1-, 3- and 5-times the maximum recommended dose to dogs with a deficient multidrug-resistance protein 1 (MDR1-/-). After repeated administration of 3- and 5-times the maximum recommended dose, mostly within 24 hours, ataxia and emesis were observed. Overall, the veterinary medicinal product was tolerated in MDR1-/- dogs following oral administration.

7. Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Vomiting[1]
Uncommon (1 to 10 animals / 1 000 animals treated):	Diarrhea[1], Hypersalivation[1], Retching[1]; Lethargy[2], Decreased appetite[2]
Rare (1 to 10 animals / 10 000 animals treated):	Blood in faeces[1]
Very rare (< 1 animal / 10 000 animals treated, including isolated reports):	Muscle tremor, Ataxia (incoordination), Convulsion[3]

[1] usually resolves within 1 day
[2] usually resolves within 2 days
[3] may be serious

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

For oral use.

Dose:
The veterinary medicinal product should be administered at a dose of 10–20 mg/kg of fluralaner and 0.75–1.5 mg/kg of milbemycin oxime in accordance with the following table:

Bodyweight (kg) of dog	**Number and strength of BRAVECTO CombiUNO chewable tablet to be administered**					
	25 mg/ 1.875 mg	50 mg/ 3.75 mg	100 mg/ 7.5 mg	200 mg/ 15 mg	400 mg/ 30 mg	600 mg/ 45 mg
1.27–2.5	1					
> 2.5–5		1				
> 5–10			1			
> 10–20				1		
> 20–40					1	
> 40–60						1

The chewable tablet should not be broken or divided.
For dogs above 60 kg appropriate combinations of chewable tablets should be used.
To ensure a correct dosage, bodyweight should be determined as accurately as possible.
Underdosing could result in ineffective use and may favour resistance development.

Method of administration:
Administer the veterinary medicinal product at or around the time of feeding.

The veterinary medicinal product is a flavoured chewable tablet. Tablets can be offered to the dog, given with food or placed directly into the mouth. The dog should be observed during administration to confirm that the full chewable tablet is swallowed.

9. Advice on correct administration

Treatment:
For infestations with ticks, fleas, gastrointestinal nematodes, heartworm and lungworm, the need for and frequency of re-treatments should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Ticks and fleas:
For optimal treatment and control of flea and tick infestation, the veterinary medicinal product should be administered at intervals of 1 month.

Gastrointestinal nematodes:
For the concurrent treatment of infections with gastrointestinal nematodes, a single dose of the product should be administered. Where necessary, dogs can be re-treated at 1-month intervals.

Heartworm:
The veterinary medicinal product kills *Dirofilaria immitis* larvae up to one month after their transmission. Therefore, the veterinary medicinal product should be administered at regular monthly intervals during the time of the year when vectors (mosquitoes) are present. Administration should start in the month after the first expected exposure to the vectors and should continue until 1-month after the last exposure to the vectors.
Dogs in areas endemic for heartworm, or dogs which have travelled to endemic areas, may be infected with adult heartworms. Therefore prior to administration of the veterinary medicinal product for the concurrent prevention of infection with adult *D. immitis*, the advice provided in section 6 should be considered.

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 4 months 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.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 30 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the packaging 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.
This veterinary medicinal product should not enter water courses as fluralaner and milbemycin oxime 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.

14. Marketing authorisation numbers and pack sizes

PVC-oPA-aluminium-oPA-PVC foil blister sealed with PET-aluminium foil lid.

Each blister strip contains one chewable tablet.

Pack sizes:

Cardboard box containing 1 blister strip with 1 chewable tablet
Cardboard box containing 3 blister strips with 1 chewable tablet each
Cardboard box containing 6 blister strips with 1 chewable tablet each

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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:
Intervet International B.V., Wim de Körverstraat 35, 5831 AN Boxmeer, The Netherlands

Manufacturer responsible for batch release:
Intervet Ges.m.b.H., Siemensstrasse 107, 1210 Vienna, Austria

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

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17. Other information

The product contributes towards the control of the environmental flea populations in areas to which treated dogs have access.
The onset of effect is within 12 hours for fleas (*C. felis*) and 24 hours of attachment for *R. sanguineus* and 24 hours for *D. reticulatus* ticks.
Fluralaner reduces the risk of infection with *Babesia canis canis* via transmission by *D. reticulatus* by killing the ticks before disease transmission occurs.
Fluralaner reduces the risk of infection with *Dipylidium caninum* via transmission by *C. felis* by killing the fleas before disease transmission occurs.