SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BRAVECTO TriUNO chewable tablets for dogs (> 40-60 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Active substances:

BRAVECTO TriUNO chewable tablets for dogs	Fluralaner (mg)	Moxidectin (mg)	Pyrantel (as embonate) (mg)
> 40-60 kg	600	1.5	300

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Cellulose, microcrystalline (Type 101)	
Cellulose, microcrystalline porous	
Cellulose, microcrystalline (Type 102)	
Croscarmellose sodium	
Pigment blend PB-565041 Brown	
Hypromellose	
Water, purified	
Poloxamer P188	
Magnesium aluminometasilicate	
Magnesium carbonate, light	
Ethanol, anhydrous	
Pork liver flavour	
Silica, colloidal anhydrous	
Magnesium stearate	
Sodium lauril sulfate	
Butylated hydroxytoluene (E321)	0.1%

Light pink to light brown coloured, mottled, round-shaped chewable tablets.

3. CLINICAL PARTICULARS

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, one or more of the target gastrointestinal nematodes, and prevention of either heartworm or lungworm disease, are all indicated at the same time.

For the treatment of tick and flea infestations in dogs providing immediate and persistent flea (*Ctenocephalides felis* and *C. canis*) and 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 veterinary medicinal 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 veterinary medicinal product's activity against the vector.

Treatment of infections with gastrointestinal nematodes of the following species: roundworms (adult stages of *Toxocara canis* and *Toxascaris leonina),* hookworms (L4, immature adult (L5) and adult stages of *Ancylostoma caninum* and adult stages of *Uncinaria stenocephala*).

Prevention of heartworm disease (caused by *Dirofilaria immitis*).

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

3.3 Contraindications

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

3.4 Special warnings

Use of this combination veterinary medicinal product should be restricted to situations where all active substances are necessary at the time of administration. In the absence of a risk of co-infection with both ecto- and endoparasites, a narrow spectrum product should be used.

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to a reduction in efficacy. In each individual animal the decision to use this veterinary medicinal product should be based on confirmation of the parasitic species present and their burden, or the risk of infestation/infection based on the epidemiological features of the specific case.

Parasites need to start feeding on the host to become exposed to fluralaner; therefore, the risk of the transmission of parasite borne diseases (including *Babesia 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 *D. immitis* has been established. It is therefore recommended, in accordance with good veterinary practice, that all animals 6 months of age or more, living in, or have travelled to, areas where a vector exists, should be tested for existing adult heartworm infections before beginning preventive use with the veterinary medicinal product.

Furthermore, it is essential that the guidance set out in section 3.9 (Amount(s) to be administered and administration route) is followed closely and that there are no gaps in product use for the prevention of heartworm disease while an animal is exposed to the parasite's vector.

For the treatment of infections with gastrointestinal nematodes the need for re-treatment should be evaluated by the prescribing veterinarian. When re-treatment is considered necessary, the choice of the treatment (monosubstance or combination product) and the frequency of use should be determined by the responsible veterinarian.

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

3.5 Special precautions for use

Special precautions for safe use in the target species:
In the absence of available data, treatment of puppies less than 8 weeks of age should be based on a benefit-risk assessment by the responsible veterinarian.

In (MDR1-/-) dogs, the safety of the veterinary medicinal product was investigated in a laboratory study following the administration of only a single dose. At a single observation timepoint, depression was observed in one animal given the maximum recommended dose. At 3 and 5 times the maximum recommended dose, depression was observed in multiple animals in a dose-related manner. The recommended dose should be strictly observed in MDR1 mutant (-/-) dogs with a non-functional P-glycoprotein, which may include Collies and related breeds.

Use with caution in dogs with pre-existing epilepsy.

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:
Accidental ingestion of a tablet by a child may cause symptoms such as headache or nausea.
Keep tablets in the original packaging until use in order to prevent children from getting access to the product and ensure that if the tablet is administered via the dog's feed, that it is fully consumed.
In case of accidental ingestion by a child, seek medical advice immediately and show the package leaflet or the label to the physician.
The product may cause skin or eye irritation.
Should skin or eye irritation occur, rinse the affected area with water. If irritation persists, seek medical advice.
Pyrantel may cause hypersensitivity reactions. People with sensitivity to pyrantel should avoid contact with the product. If symptoms such as a skin rash occur, seek medical advice.
Do not eat, drink, or smoke while handling the product.
Wash hands after use.

Special precautions for the protection of the environment:
The active substances, fluralaner and moxidectin, are mostly excreted in the faeces and may be toxic to non-target organisms. In order to avoid contamination of the environment, dog faeces should be bagged up and disposed of safely.

3.6 Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Digestive tract disorders (e.g. diarrhoea, emesis)[1]
Uncommon (1 to 10 animals / 1,000 animals treated):	Lethargy[2], Hypersalivation[1], Decreased appetite
Very rare (<1 animal / 10,000 animals treated, including isolated reports)	Muscle tremors, ataxia, convulsions[3]

[1] Mild and usually resolves within 1 day
[2] Mild and 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.

Laboratory studies with moxidectin in rats and mice have shown evidence of foetotoxic and teratogenic effects.

Fertility:
Do not use in breeding animals

3.8 Interaction with other medicinal products and other forms of interaction

Macrocyclic lactones including moxidectin have been shown to be substrates for p-glycoprotein. 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

Oral use.

Dose:
The veterinary medicinal product should be administered orally at a dose of 10-20 mg/kg of fluralaner, 0.025-0.05 mg/kg moxidectin and 5-10 mg/kg of pyrantel in accordance with the following table:

Bodyweight of dog (kg)	**Number and strength of chewable tablet to be administered**					
	BRAVECTO TriUNO 25/0.0625/ 12.5 mg	BRAVECTO TriUNO 50/0.125/ 25 mg	BRAVECTO TriUNO 100/0.25/ 50 mg	BRAVECTO TriUNO 200/0.5/ 100 mg	BRAVECTO TriUNO 400/1/ 200 mg	BRAVECTO TriUNO 600/1.5/ 300 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 and chewable tablet. If the tablet is not taken up voluntarily by the dog it can also be given with food or 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 re-treatment should be based on the advice of the prescribing veterinarian. Use of this veterinary medicinal product should take into consideration the local epidemiological situation, the animal's lifestyle, and the prudent use principles set out under Special Warnings (see section 3.4).

Ticks and fleas:
For optimal treatment and control of flea and tick infestations, the veterinary medicinal product should be administered at intervals of 1-month, provided that repeated use is prudent based on the principles set out under Special Warnings (see section 3.4).

Gastrointestinal nematodes:
The treatment of concurrent infections with gastrointestinal nematodes is achieved by administering a single dose of the veterinary medicinal product. When the ongoing use of the veterinary medicinal product is indicated (see section 3.2), re-administration to dogs at 1-month intervals is also appropriate for repeated treatment of gastrointestinal nematodes.

Heartworm:
The veterinary medicinal product kills *Dirofilaria immitis* larvae that have been transmitted within the previous month. Therefore, for the prevention of heartworm (*D. immitis*), 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. When replacing another heartworm preventative product in a heartworm prevention programme, the first treatment with the veterinary medicinal product must be given within 1-month of the last dose of the former medication.
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 prevent angiostrongylosis by reducing the level of infection with immature adults (L5) and adult stages 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 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 in 8-weeks old healthy puppies administered with up to 5 times the maximum recommended dose for 7 consecutive doses over six monthly intervals.

In a laboratory study, the veterinary medicinal product was administered once at 3 and 5 times the maximum recommended dose to dogs with a deficient multidrug-resistance protein 1 (*MDR1-/-*). Within 24 hours, dose related neurological signs (mainly depression) and emesis, were observed at all doses administered. After administration of a single overdose at 5 times the maximum recommended dose, transient neurological signs (mainly depression, ataxia, and muscle fasciculations) of mild (occasionally moderate) severity 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: QP54AB52

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.

For fleas, the onset of efficacy is within 24 hours of attachment, for 30 days after the veterinary medicinal product's administration.

Fluralaner reduces the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* by killing the ticks within 36 hours, before disease transmission occurs.

Fluralaner reduces the risk of infection with *D. caninum* via transmission by *C. felis* by killing the fleas within 24 hours, 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 flea and fly, fluralaner is not affected by dieldrin resistance.

In vitro, using a variety of different bio-assays, fluralaner was not affected by proven field resistances against amidines (tick), organophosphates (tick), cyclodienes (tick, flea), macrocyclic lactones, phenylpyrazoles (tick, flea), benzophenyl ureas (tick), pyrethroids (tick) and carbamates (tick).

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 flea life cycle is therefore broken.

New flea infestations are prevented by the rapid onset of action and long-lasting efficacy against adult fleas on the animal and the absence of viable egg production. The veterinary medicinal product therefore also contributes towards the control of environmental flea populations in areas to which treated dogs have access.

Moxidectin
Moxidectin, a semisynthetic derivative of nemadectin, belongs to the milbemycin group of macrocyclic lactones (avermectins being the other). Milbemycins and avermectins have a common mode of action that is based on the binding of ligand-gated chloride channels (glutamate-R and GABA-R). This leads to an increased membrane permeability of nematode and arthropod nerve and/or muscle cells for chloride ions and results in hyperpolarisation, paralysis and death of the parasites. Binding of glutamate-gated chloride channels, which are specific to invertebrates and do not exist in mammals, is considered the main mechanism for the anthelmintic and insecticidal activity. Moxidectin has parasiticidal activity against a range of internal and external parasites (including nematodes (*Toxocara canis, Toxascaris leonina, Ancylostoma caninum* and *Uncinaria stenocephala*), lungworm (*Angiostrongylus vasorum*) and heartworm (*Dirofilaria immitis*)). Moxidectin lacks substantial efficacy against fleas and ticks.

Pyrantel
Pyrantel belongs to the class of tetrahydropyrimidines and targets nicotinic acetylcholine channel receptors (nAChRs). Selectivity of pyrantel for invertebrate nAChRs is based on high-affinity binding to specific nematode receptor subtypes and a subsequent agonistic mode of action leading to a depolarizing neuromuscular block, which causes muscle contraction, paralysis, and subsequently death of the parasites. Pyrantel lacks activity against muscarinic mAChRs. Pyrantel is an anthelmintic with parasiticidal activity against gastrointestinal parasites (including *T. canis, T. leonina, A. caninum* and *U. stenocephala*).

4.3 Pharmacokinetics

Fluralaner is readily and rapidly absorbed systemically following oral dosing, reaching mean maximum concentrations in plasma within 17.7 hours (T_{max}) after administration.

Fluralaner is slowly eliminated from plasma (half-life of approximately 12 days) via biliary excretion and elimination through the faeces with minor contributions of metabolic clearance. A fed prandial state of the dog increases the extent of absorption of fluralaner.

Moxidectin is readily and rapidly absorbed systemically following oral dosing, reaching mean maximum concentrations in plasma within 3 hours (T_{max}) after administration. Moxidectin is slowly eliminated from plasma (half-life of approximately 16 days) via biliary excretion and elimination through the faeces with minor contributions of metabolic clearance.

Pyrantel is poorly absorbed, and the absorbed portion has a T_{max} of 1.5 hours and half-life of 6 hours. Pyrantel is eliminated through faeces and the small, absorbed portion is eliminated mainly via urine.

The pharmacokinetic profiles of fluralaner, moxidectin and pyrantel are not affected by co-administration.

No accumulation of pyrantel was observed after six repeated monthly administrations of the veterinary medicinal product at the maximum recommended dose. However, accumulation of fluralaner was observed up to and including the 6th monthly administration. Additionally, accumulation of moxidectin was observed up to and including the 5th monthly 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 ºC.

5.4 Nature and composition of immediate packaging

Carton with aluminium foil blister sealed with PET aluminium foil lid stock.
One cardboard box contains 1, 3 or 6 chewable tablets.
Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater.

The veterinary medicinal product should not enter water courses as fluralaner and moxidectin 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

MSD Animal Health UK Limited

7. MARKETING AUTHORISATION NUMBER

Vm 01708/5121

8. DATE OF FIRST AUTHORISATION

06 March 2025

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

March 2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the ‘Product Information Database’ on www.gov.uk.

Gavin Hall

Approved: 15 April 2025