SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 1,400 mg chewable tablets for very large dogs (>40 – 56 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each chewable tablet contains:

Bravecto chewable tablets	Fluralaner (mg)
for very large dogs (>40 – 56 kg)	1,400

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablet.
Light to dark brown tablet with a smooth or slightly rough surface and circular shape. Some marbling, speckles or both may be visible.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For the treatment of tick and flea infestations in dogs.

This veterinary medicinal product is a systemic insecticide and acaricide that provides:
- immediate and persistent flea (*Ctenocephalides felis*) killing activity for 12 weeks,
- immediate and persistent tick killing activity for 12 weeks for *Ixodes ricinus, Dermacentor reticulatus* and *D. variabilis,*
- immediate and persistent tick killing activity for 8 weeks for *Rhipicephalus sanguineus,*
- persistent tick killing activity from 7 days to 12 weeks after treatment for *Ixodes hexagonus.*

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).
For the treatment of demodicosis caused by *Demodex canis*.
For the treatment of sarcoptic mange (*Sarcoptes scabiei* var. *canis*) infestation.

For reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for up to 12 weeks. 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 *Ctenocephalides felis* for up to 12 weeks. The effect is indirect due to the product's activity against the vector.

4.3 Contraindications

Do not use in cases 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 fluralaner; therefore the risk of the transmission of parasite borne diseases (including *Babesia canis canis* and *D. caninum*) cannot be completely excluded.

Unnecessary use of antiparasitics or use deviating from the instructions given may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.

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

4.5 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, the veterinary medicinal product should not be used on puppies less than 8 weeks old and /or dogs weighing less than 2 kg.
The product should not be administered at intervals shorter than 8 weeks as the safety for shorter intervals has not been tested.

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

Keep the product in the original packaging until use, in order to prevent children from getting direct access to the product.
Hypersensitivity reactions in humans have been reported.
Do not eat, drink or smoke while handling the product.
Wash hands thoroughly with soap and water immediately after use of the product.

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

Other precautions:
Not applicable.

4.6 Adverse reactions (frequency and seriousness)

Dogs

Common (1 to 10 animals / 100 animals treated):	Gastrointestinal effects (Anorexia, Hypersalivation, Diarrhoea, Emesis)*#.
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Lethargy** Muscle tremor**, Ataxia**, Convulsion**.

* observed in clinical trials

**reported during post marketing safety experience, self-limiting and of short duration
mild and transient

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See also the last section of the package leaflet for respective contact details.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product in breeding, pregnant and lactating dogs has been demonstrated. Can be used in breeding, pregnant and lactating dogs.

4.8 Interaction with other medicinal products and other forms of interaction

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 Bravecto chewable tablets for dogs and routinely used veterinary medicinal products were observed.

4.9 Amount(s) to be administered and administration route

For oral use.

The veterinary medicinal product should be administered in accordance with the following table (corresponding to a dose of 25 – 56 mg fluralaner/kg bodyweight within one weight band):

Bodyweight of dog (kg)	Strength and number of tablets to be administered				
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg	Bravecto 1,000 mg	Bravecto 1,400 mg
2 – 4.5	1				
>4.5 – 10		1			
>10 – 20			1		
>20 – 40				1	
>40 – 56					1

The chewable tablets should not be broken or divided.
For dogs above 56 kg body weight, use a combination of two tablets that most closely matches the bodyweight.
Underdosing could result in ineffective use and may favour resistance development.

Method of administration
Administer Bravecto chewable tablets at or around the time of feeding.
Bravecto is a chewable tablet and is well accepted by most dogs. 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 tablet is swallowed.

Treatment schedule
For optimal control of flea infestation, the veterinary medicinal product should be administered at intervals of 12 weeks. For optimal control of tick infestation, the timing of retreatment depends on the tick species. See section 4.2.
For the treatment of *Demodex canis* mite infestations, a single dose of the product should be administered. As demodicosis is a multi-factorial disease, it is advisable to also treat any underlying disease appropriately.
For the treatment of sarcoptic mange infestations *(Sarcoptes scabiei* var*. canis)*, a single dose of the product should be administered. The need for and frequency of re-treatment should be in accordance with the advice of the prescribing veterinarian.

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 2.0 – 3.6 kg treated with overdoses of up to 5 times the maximum recommended dose (56 mg, 168 mg and 280 mg fluralaner/kg body weight) on three occasions at shorter intervals than recommended (8-week intervals).

There were no findings on reproductive performance and no findings of concern on offspring viability when fluralaner was administered orally to Beagle dogs at overdoses of up to 3 times the maximum recommended dose (up to 168 mg/kg body weight of fluralaner).

The veterinary medicinal product was well tolerated in Collies with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 3 times the recommended dose (168 mg/kg body weight). No treatment-related clinical signs were observed.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use.
ATCvet code: QP53BE02.

5.1 Pharmacodynamic properties

Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Ixodes* spp., *Dermacentor* spp. and *Rhipicephalus sanguineus*), fleas (*Ctenocephalides* spp.), *Demodex canis* mites and sarcoptic mange (*Sarcoptes scabiei* var. *canis*) on the dog.

Fluralaner reduces the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* by killing the ticks within 48 hours, before disease transmission occurs.

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

The onset of effect is within 8 hours of attachment for fleas (*C. felis*) and 12 hours of attachment for *I. ricinus* and 48 hours for *D. reticulatus* ticks. The onset of acaricidal efficacy against *I. hexagonus* ticks was demonstrated 7 days after treatment.

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 *in vitro* bio-assays, 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 (mite).

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

5.2 Pharmacokinetic particulars

Following oral administration, fluralaner is readily absorbed reaching maximum plasma concentrations within 1 day. Food enhances the absorption. Fluralaner is systemically distributed and reaches the highest concentrations in fat, followed by liver, kidney and muscle. The prolonged persistence and slow elimination from plasma ($t_{1/2}$ = 12 days) and the lack of extensive metabolism provide effective concentrations of fluralaner for the duration of the inter-dosing interval. Individual variation in C_{max} and $t_{1/2}$ was observed. The major route of elimination is the excretion of unchanged fluralaner in faeces (~90% of the dose). Renal clearance is the minor route of elimination.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pork liver flavour
Sucrose
Maize starch
Sodium lauryl sulfate
Disodium pamoate monohydrate
Magnesium stearate
Aspartame
Glycerol
Soya-bean oil
Macrogol 3350

6.2 Major 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 veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 aluminium foil blister sealed with PET aluminium foil lid stock containing 1, 2 or 4 chewable 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

Medicines should not be disposed of via wastewater.

The veterinary medicinal product should not enter water courses as fluralaner may be dangerous for aquatic invertebrates.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MSD Animal Health UK Limited
Walton Manor, Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

8. MARKETING AUTHORISATION NUMBER

Vm 01708/5019

9. DATE OF FIRST AUTHORISATION

11 February 2014

10. DATE OF REVISION OF THE TEXT

May 2023

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Approved 24 January 2024