EXTEND YOUR PARALYSIS TICK AND FLEA PROTECTION

1 Tasty Chew. 3 MONTHS PROTECTION.*

- 3 MONTHS AGAINST FLEAS
- 4 MONTHS AGAINST PARALYSIS TICKS

*Refer to label for full claim details.
FLEA AND TICK MANAGEMENT MAY BE A CHALLENGE FOR DOG OWNERS

- Monthly and fortnightly treatments require diligent reapplication.
- Inconsistently applied treatments can leave dogs vulnerable to parasite risks.
- The majority of dog owners only treat for fleas and ticks every 3 months or less frequently.\(^1\)
- Protection gaps can lead to reinfestation.
- Topically applied products may wash or rub off.

### FLEA AND TICK TREATMENT COMPLIANCE AMONGST DOG OWNERS

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Flea</th>
<th>Tick</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Less often</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>Annually</td>
<td>31%</td>
<td>13%</td>
</tr>
<tr>
<td>Every 6 months</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Every 3 months</td>
<td>39%</td>
<td>28%</td>
</tr>
<tr>
<td>Every month</td>
<td>34%</td>
<td>34%</td>
</tr>
<tr>
<td>Fortnightly</td>
<td>6%</td>
<td>4%</td>
</tr>
</tbody>
</table>

57% of owners treat their dog for fleas every 3 months or less frequently\(^1\)
62% of owners treat their dog for ticks every 3 months or less frequently\(^1\)

NOW IS THE TIME FOR A SMART SOLUTION.
BRAVECTO
A QUANTUM LEAP FORWARD IN PET SCIENCE

BRAVECTO (FLURALANER) IS A MEMBER OF THE ISOXAZOLINE CLASS OF PARASITICIDES.

UNIQUE MODE OF ACTION
• Fluralaner is a potent inhibitor of parts of the arthropod nervous system.¹,³
• It acts antagonistically on two different ligand-gated chloride channels (GABA-receptor and glutamate-receptor).²
• Fluralaner has selective inhibitory activity on insecticidal/acaricidal targets.³
  - Fluralaner has less pronounced activity on the tested mammalian GABA-receptor indicating a high safety margin.⁴
  - Inhibitory glutamate-gated chloride channels exist in arthropods, not in mammals.³

NOT IMPACTED BY KNOWN RESISTANCES
• In vitro studies show high efficacy against flea strains which are resistant to several classes of ectoparasiticides including the phenyl pyrazole class (e.g. fipronil).²,⁴,⁵
• An in vivo study also showed Bravecto is effective against fipronil-resistant strains of fleas.⁴
• In a recent in vitro study, fluralaner also exhibited higher parasiticidal activity compared with fipronil, imidacloprid and other agents with different modes of action.²

EXCLUSIVE TO ANIMAL HEALTH
• Developed specifically for veterinary use and has not been used in crop protection.
• Oral administration of fluralaner achieves rapid anti-parasitic activity and has extended duration.
  - Rapid absorption ($T_{\text{max}}$ - 1 day).\(^6\)
  - Long elimination half-life ($T_{1/2}$ 12-15 days).\(^6\)
  - Quantifiable plasma concentrations for $\geq$ 12 weeks.\(^6\)
  - High distribution to tissues and low clearance, explains the long-lasting systemic availability of fluralaner in dogs.\(^6\)
  - No major metabolism and excretion mainly via faeces.\(^5\)
  - Feeding increases the bioavailability of fluralaner.\(^7\)
EXTENDED PROTECTION

- Treatment and prevention of flea (*Ctenocephalides felis*) infestations for three months.
- Treatment and control of paralysis tick (*Ixodes holocyclus*) for four months.
- Treatment and control of brown dog tick (*Rhipicephalus sanguineus*) for eight weeks.

Research indicates most pet owners don’t use insecticides year-round.¹

Flea and tick treatments are often applied infrequently by dog owners, with some treating only every 3 months or less.¹³¹⁰

Once a flea infestation has been established it can take up to 8 or more weeks to eradicate it.⁸

The Bravecto treatment program means dog owners have little to think about and less to remember, when protecting against fleas and paralysis ticks.
RAPID AND CONSISTENT FLEA EFFICACY\textsuperscript{4,13}

- Provides effective control within 8 hours after treatment\textsuperscript{4,13}
- Continues to effectively kill newly arriving fleas within 8 hours of infestation, throughout the entire 3 month treatment interval\textsuperscript{4,13}
- Rapid onset of action kills newly emerged adult fleas before they lay eggs.
  - An \textit{in vitro} study has demonstrated that very low concentrations of fluralaner have been shown to stop the production of viable eggs by fleas\textsuperscript{4,14}

A field study\textsuperscript{4} conducted in South East Queensland, during the active flea season included 23 dogs of various breeds and weights from 17 households. The arithmetic mean flea count was 64 (range 9-259). No other insecticides on the pet or in the environment were allowed.

A single treatment with Bravecto on visit 1 (day 0) achieved 100% efficacy at 4 weeks post-treatment. This was maintained until the end of the study, at 12 weeks post-treatment.
ONE DOSE DOES WHAT SOME OTHER PRODUCTS DO WITH THREE

**EUROPEAN AND US FIELD STUDIES**

A randomised, blinded, multi-site European field study\(^1\), compared the efficacy of a single oral dose of Bravecto with three sequential topical treatments of fipronil at four week intervals.

**The proportion of flea-free households in the Bravecto group was significantly superior to the fipronil-treated households at all time points.**

In a US field study\(^1\) of 157 households with 294 client owned dogs in which flea control was assessed, pet dogs received either one dose of Bravecto (25-56mg/kg fluralaner) or three monthly doses of Comfortis\(^\circledR\) (30-60mg/kg spinosad) combined with a Preventic\(^\circledR\) (9% amitraz) collar.

**FLEA CONTROL WITH BRAVECTO VS COMFORTIS + PREVENTIC**

<table>
<thead>
<tr>
<th>WEEK</th>
<th>BRAVECTO % FLEA REDUCTION</th>
<th>CONTROL GROUP COMFORTIS + PREVENTIC % FLEA REDUCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEEK 4</td>
<td>99.7</td>
<td>96.1</td>
</tr>
<tr>
<td>WEEK 8</td>
<td>99.8</td>
<td>99.5</td>
</tr>
<tr>
<td>WEEK 12</td>
<td>99.8</td>
<td>99.6</td>
</tr>
</tbody>
</table>

\(^*\) statistically significant

**Consistently More Flea Free Dogs Seen With Bravecto**

- WEEK 4: 44.7% vs 91.1%
- WEEK 8: 88.2% vs 95.4%
- WEEK 12: 84.4% vs 95.3%

\(^*\) *statistically significant

\(\ast\) Fipronil reapplied on day 28 and again on day 56, per EU label claim.

Note: Fipronil is a registered trademark of Elanco. Preventic is a registered trademark of Virbac.
BRAVECTO REDUCES THE INCIDENCE OF FLEA ALLERGY DERMATITIS (FAD)⁴,¹¹,¹²

- Australian, US and European field studies demonstrated that one dose of Bravecto provided substantial reduction in clinical signs of flea allergy dermatitis,⁴¹¹,¹²
- Additionally, Bravecto was used in an Australian dermatologist-run study⁴ with 20 client-owned dogs, where no additional flea or flea premise products, corticosteroids or antihistamines were used.
  - At Week 4, only one flea was found on one of the enrolled dogs.
  - No fleas were found on any dogs at the Week 8 and Week 12 flea counts.
  - At week 12, after 1 administration of Bravecto, all dogs were flea free and there was 100% resolution of FAD. CADESI and pruritus scores were also significantly reduced.

100% flea free  
96.3% reduction in CADESI* score  
94.5% reduction in pruritus  
100% FAD resolution

*Canine Atopic Dermatitis, Extent and Severity Index
Toxin secretion from *Ixodes holocyclus* ticks has a specific timing during the engorgement process and is associated with major physiological changes in tick salivary glands occurring on the third day.\(^1\)\(^5\),\(^1\)\(^6\)

Laboratory dogs infested with 3 to 4 ticks had an onset of clinical signs of toxicity between 5.5 and 7 days (mean = 6.2 days) with death occurring in a mean of 23.3 hours after the onset of signs.\(^1\)\(^7\)

Therefore, to prevent the occurrence of fatal paralysis in tick infested dogs, it is critical to kill the ticks within 72 hours post infestation and prior to the onset of clinical signs.

**TREATS AND CONTROLS PARALYSIS TICK FOR 4 MONTHS**\(^4\)

- Bravecto provides effective control of pre-existing paralysis ticks (*Ixodes holocyclus*) within 24 hours of treatment.\(^4\)
- Bravecto also controls brown dog tick (*Rhipicephalus sanguineus*) for 8 weeks.
- In tick season daily searching for and removal of any ticks found is recommended.
- Due to the systemic nature of action of Bravecto, dead attached ticks can still be seen on animals following treatment. These ticks will often appear partially engorged. Dead ticks can be easily removed as opposed to live ticks which take some force to dislodge from the skin of the animals.
• Fluralaner efficacy against Ixodes holocyclus was >99.2% at 48 hours and 100% at 72 hours after tick infestation at all time-points post treatment, for 115 days delivering unmatched, extended protection in dogs against paralysis ticks from a single oral treatment.

• The differences between mean live tick counts on treatment and control groups were significant (P < 0.001) at all assessment time points.

In an Australian study, 24 healthy Foxhound and Foxhound cross dogs immunized against holocyclotoxin were randomly allocated to receive Bravecto treatment or no treatment.

All dogs were penned individually and 30 adult unfed female Ixodes holocyclus were individually attached 1 day before treatment and 14, 28, 42, 56, 70, 84, 112 and 140 days following treatment.

Ticks were counted and assessed at 24, 48 and 72 hours after the initial treatment and after each subsequent infestation.

Ticks were not removed at the 24 and 48 hour assessments, but were removed after the 72 hour assessments.

Fluralaner efficacy against Ixodes holocyclus was >99.2% at 48 hours and 100% at 72 hours after tick infestation at all time-points post treatment, for 115 days delivering unmatched, extended protection in dogs against paralysis ticks from a single oral treatment.

The differences between mean live tick counts on treatment and control groups were significant (P < 0.001) at all assessment time points.
REASSURANCE FOR YOU AND YOUR CUSTOMERS

- Bravecto can be used in puppies from 8 weeks of age weighing greater than 2kg.
- Bravecto has been shown to be well tolerated in puppies when tested at up to 5X the highest recommended treatment dose (280 mg fluralaner/kg BW) on 3 occasions at 8-weeks intervals.4,18
- Bravecto can be used in breeding, pregnant and lactating dogs.
- Bravecto is well tolerated in MDR1 gene deficient collies. Following a single administration at 3 times the highest recommended treatment dose in clinical use (168 mg/kg BW), no treatment-related clinical signs were observed.19
- During clinical field testing, no interactions between Bravecto and routinely used medicinal products were observed.4,11,12
- In the US field trial the most common adverse event in the Bravecto treated group was vomiting, seen in a small number of dogs (7.1%) over a 26 week period, compared with 14.3% over a 12 week period in the oral Comfortis plus Preventic collar treated control group.12 In the EU field study, adverse events were limited to mild and transient gastrointestinal signs such as diarrhoea and vomiting in 1% of Bravecto treated dogs. 2.3% of Frontline treated dogs had primarily dermal adverse events.11
EASY TO GIVE, LESS TO THINK ABOUT

• A highly palatable, easy to administer chew - studies show more than 91.7% of dogs accept Bravecto voluntarily.4,12
• Bravecto’s extended protection periods* mean clients have few treatments to remember each year, therefore less to forget.
• No mess to administer, no liquids to spill or transfer.
• Full year flea protection in just four tasty doses - protection at every season. Fits easily into gastrointestinal worming programs where treatments occur every 3 months.

Bravecto is ideal for active dogs with a love of swimming, or dogs with skin conditions that require frequent bathing, due to its systemic activity.

1 Tasty Chew. 3 MONTHS PROTECTION.*

*3 months protection against fleas, 4 months protection against paralysis ticks and 8 weeks protection against brown dog ticks. Refer to label for full claim details.
**SIMPLE DOSING FOR INCREASED CONVENIENCE**

- Within each weight range, a whole tablet must be used. For dogs weighing more than 56kg use a combination of tablets that most closely matches the bodyweight.
- Administer Bravecto at or around the time of feeding for maximum bioavailability.\(^7\)
- In dogs older than 8 weeks, treatment every 8 weeks has been shown to be well tolerated.

<table>
<thead>
<tr>
<th>Bodyweight of dog (kg)</th>
<th>B BRAVECTO® 112.5 mg</th>
<th>B BRAVECTO® 250 mg</th>
<th>B BRAVECTO® 500 mg</th>
<th>B BRAVECTO® 1000 mg</th>
<th>B BRAVECTO® 1400 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 - 4.5</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;4.5 - 10</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;10 - 20</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;20 - 40</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;40 - 56</td>
<td>1</td>
<td></td>
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</tbody>
</table>

**EASY TO MERCHANDISE IN SINGLE DOSE PACKS**
THE ONLY ORAL CHEW TO DELIVER 3 MONTHS FLEA AND 4 MONTHS PARALYSIS TICK PROTECTION FOR DOGS IN A SINGLE DOSE.

For further information or to order Bravecto® contact your MSD Animal Health representative or call the Bravecto Hotline on 1800 230 833.