FOR ANIMAL USE ONLY

BRAVECTO®

For Miniature Dogs	(2 – 4,5 kg)
For Small Dogs	(> 4,5 – 10 kg)
For Medium Dogs	(> 10 – 20 kg)
For Large Dogs	(> 20 – 40 kg)
For Extra-Large Dogs	(> 40 – 56 kg)

Reg. No. G4083 (Act 36/1947)
Namibia Reg. No. V14/18.3.10/1259 NS0

This product may only be sold by persons registered in terms of section 23(1) (c) of the Veterinary and Para-Veterinary Professions Act, 1982 (Act No. 19 of 1982).

INDICATIONS
For the treatment and prevention of tick, flea and mite infestations in dogs. **Bravecto®** kills adult, as well as juvenile ticks (larvae and nymphs). **Bravecto®** can be used as part of a treatment strategy for Flea Allergy Dermatitis (FAD). For the treatment of Demodicosis caused by *Demodex* spp. and Sarcoptic mange mites. In a controlled trial, treatment with fluralaner resulted in the complete removal of *Demodex* spp. mites from treated dogs. For the treatment of *Otodectes* spp. mite infestations.

COMPOSITION
Contains fluralaner equivalent to 25 to 56 mg/kg body weight.
Each chewable tablet contains:

Miniature Dogs:	112,5 mg
Small Dogs:	250 mg
Medium Dogs:	500 mg
Large Dogs:	1 000 mg
Extra-Large Dogs:	1 400 mg

CAUTION

STORAGE
Store at or below 30 °C in a cool, dry place.

PHARMACOLOGICAL ACTION
Pharmacodynamic properties
Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Ixodes* spp., *Dermacentor* spp., *Haemaphysalis elliptica* and *Rhipicephalus sanguineus*) and fleas (*Ctenocephalides* spp.) and mites (*Demodex* spp., *Sarcoptes* spp., *Otodectes* spp.) on dogs. Fluralaner is systemically active on target parasites. Contact activity against ticks and fleas is of minor relevance. 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 a molecular on target study, fluralaner is not affected by dieldrin resistance.
In vitro, fluralaner overcomes resistance against amidines, organophosphates, cyclodienes, macrocyclic lactones, phenylpyrazoles, benzophenyl ureas, pyrethroids and carbamates.
In vivo, fluralaner is highly effective against fleas proven to be less susceptible to phenylpyrazole insecticides.

Pharmacokinetic properties
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 the visceral fat, followed by liver,

kidney and muscle. The prolonged persistence and slow elimination from plasma ($t_{½}$ = 12 days) and the lack of extensive metabolism provide effective concentrations of fluralaner for the duration of the inter-dosing interval, ensuring efficacy for 12 weeks. 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.

WARNINGS

- **Use with caution in dogs with pre-existing epilepsy.**
- Safety in puppies less than 8 weeks of age and/or dogs weighing less than 2 kg has not been established.
- Keep the product in the original packaging until use.
- Do not use in case of hypersensitivity to fluralaner or to any of the excipients.
- KEEP OUT OF REACH OF CHILDREN, UNINFORMED PERSONS AND ANIMALS.
- Can be used in breeding, pregnant and lactating dogs.
- **Bravecto® is well tolerated in MDR1 dogs following oral administration.**
- Although this remedy has been extensively tested under a large variety of conditions, failure thereof may ensue as a result of a wide range of reasons. If this is suspected, seek veterinary advice and notify the registration holder.

PRECAUTIONS

- Do not eat, drink or smoke while handling the product.
- Wash hands thoroughly with soap and water immediately after use of the product.
- Do not store with food, drinks, medication or household products.
- Do not administer at intervals shorter than 8 weeks as the safety for shorter intervals has not been tested.

ADVERSE REACTIONS

Commonly observed adverse reactions in clinical trials (1,6 % of treated dogs) were mild and transient gastrointestinal effects such as diarrhoea, vomiting, inappetence, and drooling.

Convulsions and lethargy have been reported very rarely in spontaneous (pharmacovigilance) reports.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1 000 animals)
- rare (more than 1 but less than 10 animals in 10 000 animals)
- very rare (less than 1 animal in 10 000 animals, including isolated reports).

DIRECTIONS FOR USE – USE ONLY AS DIRECTED

- Administer tablets at or around the time of feeding for maximum effectiveness.
- It can be mixed with food or given by hand since it is very palatable.
- For optimal control of tick and flea infestation, **Bravecto®** should be administered at a 12 week interval.
- **Bravecto®** can be administered all year round.
- The chew tablets should not be broken or divided.

DOSAGE

Weight (kg)	Tablet size
2,0 - 4,5	112,5 mg for miniature dogs
> 4,5 - 10	250 mg for small dogs
> 10 - 20	500 mg for medium dogs

> 20 - 40	1 000 mg for large dogs
> 40 - 56	1 400 mg for extra-large dogs

Within each weight range a whole tablet must be used.
For dogs weighing more than 56 kg, use a combination of 2 tablets that most closely matches the body weight.

OVERDOSE
Bravecto® was well tolerated following oral administration to puppies aged between 8 and 9 weeks and weighing between 2,0 and 3,6 kg at doses of up to 56 mg, 168 mg and 280 mg fluralaner/kg body weight (equivalent to 1, 3 and 5 times the maximum expected clinical dose) on 3 occasions at 8-week intervals. No treatment-related adverse effects were observed.
There were no findings on reproductive performance and offspring viability when up to 168 mg/kg of fluralaner (equivalent to 3 times the maximum treatment dose) was administered orally to Beagle dogs.
Bravecto® was well tolerated in Collies with MDR1-/1 following a single dose at 3 times the recommended dose.

EFFICACY
Bravecto® was shown to be effective* against fleas and various tick species.
* Efficacy > 90 to 95 %

Bravecto® is indicated for the treatment of the following:
TICKS: (*Ixodes ricinus, Ixodes hexagonus, Ixodus scapularis, Dermacentor reticulatus, Dermacentor variabilis, Haemaphysalis elliptica* and *Rhipicephalus sanguineus.)*
Directly after treatment, at least 90 % of ticks on dogs are killed within 8 hours. During the whole treatment interval, at least 90 % of ticks on dogs are killed within 12 hours.

FLEAS: (*Ctenocephalides felis)*
Directly after treatment, at least 95 % of fleas are killed within 8 hours. During the whole treatment interval, at least 95 % of fleas on dogs are killed within 12 hours.

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

Effect on immature stages
The product kills adult as well as juvenile ticks (larvae, nymphs). 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.

Control of flea infestations and Flea Allergy Dermatitis (FAD)
The flea life cycle is broken due to the rapid onset action and long lasting efficacy against adult fleas on the animal and the absence of viable egg production. **Bravecto**® effectively controls environmental flea populations in areas to which the dog has access. **Bravecto**® can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

Mites
A single oral administration of **Bravecto**® chewable tablets to dogs with *Sarcoptes* spp., *Otodectes* spp. infestations showed a 100 % reduction in live mite counts as well as a complete elimination of live mites 28 days after treatment administration. The treatment resulted in a reduction of skin lesions and increase of hair regrowth.
Single oral administration of **Bravecto**® chewable tablets is highly effective against generalised demodicosis caused by *Demodex* spp., with no mites detectable at 56 and 84 days following treatment.

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

PRESENTATION
Packaged in an aluminium foil blister with aluminium foil lid stock in an outer carton.

REGISTRATION HOLDER
Intervet South Africa (Pty) Ltd.
20 Spartan Road, Spartan
1619, RSA
Tel: +27 (0) 11 923 9300
Fax: +27 (0) 11 392 3158
www.msd-animal-health.co.za

MANUFACTURER
Intervet GmbH
Siemensstrasse 107
1210 Vienna
Austria

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16 April 2018

SLEGS VIR DIEREGEBRUIK

BRAVECTO®

Vir Miniatuur Honde	(2 - 4,5 kg)
Vir Klein Honde	(> 4,5 - 10 kg)
Vir Medium Honde	(> 10 - 20 kg)
Vir Groot Honde	(> 20 - 40 kg)
Vir Ekstra Groot Honde	(> 40 - 56 kg)

Reg. Nr. G4083 (Wet 36/1947)
Namibië Reg. Nr. V14/18.3.10/1259 NS0

Hierdie produk mag slegs verkoop word deur persone wat in terme van artikel 23 (1) (c) van die Wet op Veterinêre en Para-Veterinêre Beroepe, 1982 (Wet Nr. 19 van 1982) geregistreer is.

INDIKASIES
Vir die behandeling en voorkoming van vlooi-, bosluis- en mytbesmettings in honde. **Bravecto®** maak volwasse bosluise, sowel as onvolwasse bosluise (larwe en nimfe) dood. **Bravecto®** kan gebruik word as deel van 'n behandelingstrategie vir Vlooi Allergiese Dermatitis (VAD). Vir die behandeling van Demodicosis veroorsaak deur *Demodex* spp. en sarkoptiese skurftemyte. In 'n goed gekontroleerde studie, het behandeling met fluralaner tot gevolg gehad dat die *Demodex* spp. myte volledig verwyder was van die behandelde honde. Vir die behandeling van *Otodectes* spp. myte besmettings.

SAMESTELLING
Bevat fluralaner ekwivalent aan 25 to 56 mg/kg liggaamsgewig.
Elke koutablet bevat:

Miniatuur Honde:	112,5 mg
Klein Honde:	250 mg
Medium Honde:	500 mg
Groot Honde:	1 000 mg
Ekstra Groot Honde:	1 400 mg

VERSIGTIG

BERGING
Berg teen of benede 30 °C in 'n koel, droë plek.

FARMAKOLOGIESE WERKING
Farmakodinamiese eienskappe
Fluralaner is 'n myt- en insekdoder. Dit is effektief teen bosluise (*(Ixodes* spp., *Dermacentor* spp., *Haemaphysalis elliptica* en *Rhipicephalus sanguineus)* en vlooie *(Ctenocephalides* spp.*)* en myte *(Demodex* spp., *Sarcoptes* spp., *Otodectes* spp.*)* op honde. Fluralaner is sistemies aktief teen teikenparasiete. Kontak-aktiwiteit teen bosluise en vlooie is van min belang. Fluralaner is 'n potente inhibeerder van dele van die geleedpotiges se senuweestelsel deur antagonisties op die ligandbeheerde chloriedkanale (GABA-reseptor en glutamaat-reseptor) te werk. In 'n molekulêre teikenstudie, was fluralaner nie geaffekteer deur dieldrienweerstand nie.
In vitro oorkom fluralaner weerstand teen amidiene, organofosfate, siklodiene, makrosikliese laktone, fenielpirasole, bensofenielureas, piretroïede en karbamate.
In vivo is fluralaner hoogs effektief teen vlooie wat minder vatbaar is teen fenielpirasool insekdoders.

Farmakokinetiese eienskappe
Na orale toediening word fluralaner goed geabsorbeer en bereik maksimum plasmakonsentrasies binne 1 dag. Voedsel verhoog die absorpsie. Fluralaner word sistemies versprei en bereik die hoogste konsentrasies in die viserale vet, gevolg deur die lewer, niere en spiere. Die verlengde teenwoordigheid, stadige plasma eliminasie ($t_{½}$= 12 dae) en die gebrek aan ekstensiewe metabolisme, verskaf effektiewe konsentrasies fluralaner vir die duur van die tussendoseringsinterval. Dit verseker effektiwiteit vir 12 weke. Die hoofroete van eliminasie is die uitskeiding van onveranderde fluralaner in feses (~ 90 % van die dosis). Renale opruiming is 'n kleiner roete van uitskeiding.

WAARSKUWINGS
- **Gebruik met versigtigheid by honde wat ly aan epilepsie.**
- Veiligheid in honde jonger as 8 weke oud en/of honde wat minder as 2 kg weeg is nie vasgestel nie.
- Hou die produk in die oorspronklike verpakking tot voor gebruik.
- Moenie gebruik word in geval van hipersensitiwiteit vir fluralaner of vir enige van die hulpstowwe nie.
- HOU BUITE BEREIK VAN KINDERS, ONINGELIGTE PERSONE EN DIERE.
- Veilig in teel-, dragtige en lakterende honde.
- **In MDR1 honde word Bravecto® goed verdra na orale toediening.**
- Alhoewel hierdie middel breedvoerig onder 'n wye verskeidenheid toestande getoets is, mag dit faal as gevolg van verskeie redes. Indien dit vermoed word, raadpleeg 'n veearts en verwittig die registrasiehouer.

VOORSORGMAATREëLS
- Moenie eet, drink of rook terwyl die produk hanteer word nie.
- Was hande deeglik met seep en water onmiddellik nadat die produk gebruik is.
- Moet nie saam met voedsel, drank, medikasie of huishoudelike produkte gestoor word nie.
- Moet nie met intervalle korter as 8 weke toedien nie, aangesien die veiligheid vir korter tussenposes nie getoets is nie.

NEWE-EFFEKTE
Algemene waargenomde nadelige reaksies in kliniese toetse (1,6 % van behandelde honde) was ligte en verbygaande gastro-intestinale effekte soos diarree, braking, lusteloosheid en verhoogde speekselafskeiding.

Konvulsies en lusteloosheid is baie selde gerapporteer in spontane (produkveiligheid) verslae.

Die frekwensie van negatiewe reaksies word gedefinieer met behulp van die volgende verduideliking:
- baie algemeen (meer as 1 in 10 diere wat negatiewe reaksie (s) tydens die verloop van een behandeling toon)
- algemeen (meer as 1 maar minder as 10 in 100 diere)
- ongewoon (meer as 1 maar minder as 10 in 1000 diere)
- skaars (meer as 1 maar minder as 10 in 10 000 diere)
- baie skaars (minder as 1 in 10 000 diere, insluitend geïsoleerde verslae).

GEBRUIKSAANWYSINGS – GEBRUIK SELGS SOOS AANGEDUI
- Vir maksimum effektiwiteit, gee tablette saam of naby etenstyd.
- Dit kan met kos gemeng word of per hand gegee word aangesien dit baie smaaklik is.
- Vir optimale beheer oor vlooi- en bosluisbesmettings moet **Bravecto®** in 12 week intervalle gegee word.
- **Bravecto®** kan reg deur die jaar toegedien word.
- Die koubare tablette mag nie gebreek of verdeel word nie.

DOSIS

Gewig (kg)	Tablet grootte
2,0 - 4,5	112,5 mg vir miniatuur honde
> 4,5 - 10	250 mg vir klein honde
> 10 - 20	500 mg vir medium honde
> 20 - 40	1 000 mg vir groot honde
> 40 - 56	1 400 mg vir ekstra groot honde

’n Hele tablet moet binne elke gewigsgroep gebruik word.
Honde wat meer as 56 kg weeg, moet ’n kombinasie van 2 tablette gebruik wat die naaste aan die liggaamsgewig is.

OORDOSERING
Bravecto® was goed hanteer na orale toediening deur klein hondjies van tussen 8 en 9 weke oud en tussen 2,0 en 3,6 kg teen dosisse van 56 mg, 168 mg en 280 mg fluralaner/kg liggaamsgewig (ekwivalent aan 1, 3 en 5 keer die maksimum verwagte kliniese dosis) op 3 geleenthede met ‘n 8 week interval. Daar was geen behandelingsverwante ongewenste effekte geïdentifiseer nie.
Na die toediening van 168 mg/kg fluralaner (ekwivalent aan 3 keer die maksimum behandelingsdosis) aan Beagle honde, was daar geen afwyking in herproduseringsvermoë of die werpsel gevind nie.
Bravecto® was goed verdra in Collies met MDR1- /1 na 'n enkele dosis teen 3 keer die aanbevole dosis.

DOELTREFFENDHEID
Daar is bewys dat **Bravecto®** effektief* teen vlooie en verskeie bosluisspesies gebruik kan word.
* Effektiwiteit > 90 tot 95 %

Bravecto® is aangedui vir die behandeling van die volgende:
BOSLUISE: (*Ixodes ricinus, Ixodes hexagonus, Ixodus scapularis, Dermacentor reticulatus, Dermacentor variabilis*, *Haemaphysalis elliptica* en *Rhipicephalus sanguineus).*
Direk na behandeling is ten minste 90 % van die bosluise op die hond binne 8 ure dood.
Tydens die hele behandelingsinterval gaan ten minste 90 % van die bosluise op die hond dood binne 12 ure.

VLOOIE: (*Ctenocephalides felis)*
Direk na behandeling gaan ten minste 95 % van die vlooie op die hond binne 8 ure dood.
Tydens die hele behandelingsinterval gaan ten minste 95 % van die vlooie op die hond dood binne 12 ure.

Vlooie en bosluise moet eers aan die gasheer heg en begin eet om blootgestel te word aan die aktiewe bestanddeel.

Effek op onvolwasse stadia
Die produk maak volwasse sowel as onvolwasse bosluise (larwes en nimfe) dood. Nuut uitgebroeide vlooie op honde gaan dood voordat lewensvatbare eiers geproduseer kan word. ‘n *In vitro* studie het ook getoon dat baie lae konsentrasies fluralaner, die produksie van lewensvatbare eiers deur vlooie kan verhoed.

Beheer van vlooi-infestasies en Vlooi Allergiese Dermatitis (VAD)
Die vlooi se lewenssiklus word verbreek deur middel van die vinnige werking en die langwerkende effektiwiteit teen die volwasse vlooie op die dier, sowel as die afwesigheid van lewensvatbare eierproduksie. **Bravecto®** beheer vlooipopulasies in die omgewing effektief in

areas waartoe die hond toegang het. **Bravecto®** kan gebruik word as deel van ‘n behandelingstrategie vir Vlooi Allergiese Dermatitis (VAD).

Myte
'n Enkele orale toediening van **Bravecto®** koubare tablette aan honde met *Sarcoptes* spp. en *Otodectes* spp. besmetting het 'n 100 % verlaging in lewende myttellings, sowel as tot 'n volkome afwesigheid van lewende myte na 28 dae se behandeling gelei. Die behandeling het gelei tot 'n vermindering van velletsels en toename in teruggroei van hare.
‘n Enkele orale toediening van **Bravecto®** koubare tablette is hoogs effektief teen algemene demodikose wat veroorsaak word deur *Demodex* spp, met geen myte wat op 56 en 84 dae na behandeling voorkom nie.

IDENTIFIKASIE
Ronde, lig- tot donkerbruin koubare tablet met ’n gladde of effens growwe oppervlak. Marmering, spikkels of beide mag sigbaar wees.

AANBIEDING
Verpak in aluminiumfoelie-stolpverpakking met aluminiumfoelie-deksel in 'n buitenste kartonhouer.

REGISTRASIEHOUER
Intervet South Africa (Pty) Ltd.
Spartanweg 20, Spartan
1619, RSA
Tel: +27 (0) 11 923 9300
Faks:+27 (0) 11 392 3158
www.msd-animal-health.co.za

VERVAARDIGER
Intervet GmbH
Siemensstrasse 107
1210 Vienna
Austria

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