1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vectra 3D spot-on solution for dogs 1.5–4 kg
Vectra 3D spot-on solution for dogs > 4–10 kg
Vectra 3D spot-on solution for dogs > 10–25 kg
Vectra 3D spot-on solution for dogs > 25–40 kg
Vectra 3D spot-on solution for dogs > 40 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Dinotefuran	54 mg
Pyriproxyfen	4.84 mg
Permethrin	397 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
N-octyl-2-pyrrolidone	-
N-methylpyrrolidone	Refer to the table below

Each spot-on applicator delivers:

Weight of dog (kg)	Colour of applicator cap	Volume (ml)	Dinotefuran (mg)	Pyriproxyfen (mg)	Permethrin (mg)	N-methyl pyrrolidone
for dogs 1.5-4 kg	Yellow	0.8	44	3.9	317	q.s. 0.8 ml
for dogs > 4-10 kg	Teal	1.6	87	7.7	635	q.s. 1.6 ml
for dogs > 10-25 kg	Blue	3.6	196	17.4	1,429	q.s. 3.6 ml
for dogs > 25-40 kg	Purple	4.7	256	22.7	1,865	q.s. 4.7 ml
for dogs > 40 kg	Red	8.0	436	38.7	3,175	q.s. 8.0 ml

Pale-yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Fleas:
Treatment and prevention of flea infestation (*Ctenocephalides felis* and *Ctenocephalides canis*). The treatment prevents flea infestation for one month. It also prevents multiplication of fleas for two months after application by inhibiting egg hatching (ovicidal activity) and by inhibiting the emergence of adults from eggs laid by adult fleas (larvicidal activity).

Ticks:
The veterinary medicinal product has persistent acaricidal and repellent efficacy against tick infestations (*Rhipicephalus sanguineus* and *Ixodes ricinus* for one month, and *Dermacentor reticulatus* for up to three weeks).

If ticks are present when the veterinary medicinal product is applied, the ticks may not all be killed within the first 48 hours, but they may be killed within a week. To remove ticks, it is recommended to use an appropriate tick removal device.

Sand flies, mosquitoes and stable flies:
The treatment provides persistent repellent (anti-feeding) activity. It prevents biting from sand flies (*Phlebotomus perniciosus*), mosquitoes (*Culex pipiens, Aedes aegypti)* and from stable flies (*Stomoxys calcitrans*) for one month post-application. The treatment also provides persistent insecticidal activity for one month against mosquitoes (*Aedes aegypti*) and stable flies (*Stomoxys calcitrans).*

Reduction of the risk of infection with the parasite *Leishmania infantum* transmitted by sand flies (*Phlebotomus* spp.) for 1 month following administration. The effect is indirect due to the product's activity against the vector.

3.3 Contraindications

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

Do not use on cats. Due to their unique physiology and inability to metabolise permethrin, this veterinary medicinal product must not be used on cats. If applied to a cat, or ingested by a cat that actively grooms a recently treated dog, this veterinary medicinal product may have serious harmful effects (see section 3.5.)

3.4 Special warnings

All dogs within the household should be treated. Cats in the household should only be treated with a veterinary medicinal product authorised for use in that species.

Fleas can infest the dog's basket, bedding and regular resting areas such as carpets and soft furnishings. In case of massive flea infestation and at the beginning of the control measures, these areas should be treated with a suitable insecticide and then vacuumed regularly.

The veterinary medicinal product remains effective when treated animals are immersed in water (e.g. swimming, bathing). Water immersion repeated weekly for one month and starting 48 hours after treatment, as well as shampooing 2 weeks after treatment do not affect the efficacy of this product. However, in case of frequent shampooing, or bathing within 48 hours after treatment, the duration of activity may be reduced.

During the first 24 hours after the initial treatment application, the protection against *L. infantum* may be reduced until the active substances are distributed over the body surface of the animal. Dogs treated for the reduction of the risk of infection with *L. infantum* transmitted by sand flies (*Phlebotomus* spp.) should therefore not be exposed to environments with sand flies during the first 24 hours after the initial treatment.
Continuous monthly treatment throughout the sand fly season is required for optimal protection against *L. infantum.*

3.5 Special precautions for use

Special precautions for safe use in the target species:

This veterinary medicinal product can induce convulsions in cats that could be fatal, due to the unique physiology of this species which is unable to metabolise certain compounds, including permethrin. In

case of accidental exposure, if undesirable effects occur, wash the cat with shampoo or soap. To prevent cats from being accidentally exposed to the veterinary medicinal product, keep cats away from treated dogs until the application site is dry. It is important to ensure that cats do not groom the site of application on a dog which has been treated with this veterinary medicinal product.

In case of suspicion of dermatitis (itch and skin irritation), seek veterinary advice.

The safety of the veterinary medicinal product has not been established in dogs younger than 7 weeks or weighing less than 1.5 kg.

Care should be taken to avoid contact between the veterinary medicinal product and the eyes of the dog. If in eyes, immediately flush with water.

The attachment of a single tick as well as the feeding of a single sand fly after treatment cannot be excluded. For this reason, the transmission of infectious diseases cannot be completely excluded if conditions are favourable.

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

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

People with known hypersensitivity to any of the ingredients should avoid contact with the veterinary medicinal product.

Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. The veterinary medicinal product should not be administered by pregnant women and women suspected of being pregnant.
Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product by women of childbearing age.

This veterinary medicinal product is irritating to the eyes and skin.

To avoid adverse reactions:
- Wash hands thoroughly and immediately after use.
- Avoid contact with the skin.
- In case of accidental spillage onto skin, wash off immediately with soap and water.
- If the veterinary medicinal product accidentally gets into the eyes, they should be thoroughly flushed with water.
- Children must not handle treated dogs for at least four hours after administration of the veterinary medicinal product. It is therefore recommended to treat dogs in the evening, or before taking them for a walk.
- On the day of treatment, treated dogs should not be permitted to sleep with their owners, especially children.
- Used applicators should be disposed of immediately and not left within the sight or reach of children.

If skin or eye irritation persists, or if the veterinary medicinal product is accidentally swallowed, seek medical advice immediately and show the package leaflet or the label to the physician.
Wait for the application site to dry before allowing the treated dog to come in contact with fabrics or furnishings.

Special precautions for the protection of the environment
Treated dogs should not be allowed to enter surface water for 48 hours after treatment to avoid adverse effects on aquatic organisms (see section 5.5).

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Application site reaction[1] (e.g. Erythema, Pruritus) Discomfort[1,2] Behavioural disorder (e.g. Hyperactivity, Vocalisation, Anxiety) Neurological disorder (e.g. Muscle tremor) Systemic disorder (e.g. Lethargy, Anorexia)
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reaction[3] (e.g. Hair change (wet appearance, spiking), Residue) Digestive tract disorder (e.g. Vomiting, Diarrhoea) Ataxia (e.g. Unsteady movement) Convulsion

[1] Mild and transient. If signs persist or worsen, veterinary advice should be sought.
[2] At the application site.
[3] Transient, these signs are usually not noticeable after 48 hours.

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 in dogs during pregnancy and lactation or in animals intended for breeding.

Pregnancy and lactation:

Use only according to the benefit-risk assessment by the responsible veterinarian.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects.

Laboratory studies, with each of the components, dinotefuran, pyriproxyfen or permethrin, in rats and rabbits have not produced any evidence of maternotoxic, teratogenic or foetotoxic effects.

Dinotefuran has been shown to cross the blood-milk barrier and is excreted in the milk.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Spot-on use.
One applicator per dog.

Dosage:

The minimum recommended dose is 6.4 mg dinotefuran/kg body weight, 0.6 mg pyriproxyfen/kg body weight and 46.6 mg permethrin/kg body weight, equivalent to 0.12 ml of the veterinary medicinal product per kg body weight.

The following table shows the size of spot-on applicator to be used according to the weight of the dog:

Weight of dog (kg)	Colour of applicator cap	Volume (ml)	Applicator to be used	
1.5-4 kg	Yellow	0.8	1 applicator of	Vectra 3D for dogs 1.5-4 kg
> 4-10 kg	Teal	1.6		Vectra 3D for dogs > 4-10 kg
> 10-25 kg	Blue	3.6		Vectra 3D for dogs > 10-25 kg
> 25-40 kg	Purple	4.7		Vectra 3D for dogs > 25-40 kg
> 40 kg	Red	8.0		Vectra 3D for dogs > 40 kg

Care should be taken to apply the veterinary medicinal product only onto intact (undamaged) dog's skin.

How to apply:
Remove the spot-on applicator from the pack.

Step 1: Hold the applicator upright, placing fingers below the larger disk as shown.



Step 2: With the other hand, press downwards on the smaller disk until the 2 disks meet evenly. This will pierce the seal.



Step 3: The dog should be standing or in a comfortable position for easy application. Part the hair until the skin is visible. Apply the veterinary medicinal product (as directed in step 4 below) slowly with the tip of the applicator on the skin.



Step 4
Use according to **4a** or **4b** recommendation:

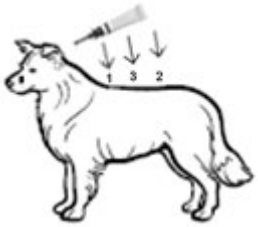
4a recommendation: Gently squeeze the applicator and apply the veterinary medicinal product to the skin along the dog's back, beginning between the shoulder blades, in the number of spots and order shown in the diagrams below and squeezing until the applicator is empty. Avoid superficial application to the dog’s hair. The number of application spots will depend on the body weight of the dog.



Dogs from 1.5 to 4 kg body weight
1 yellow pipette per dog



Dogs over 4 kg and up to 10 kg body weight
1 teal pipette per dog to be split in 2 spots

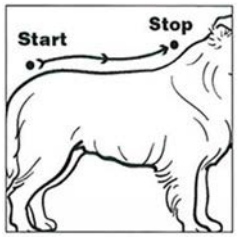


Dogs over 10 kg and up to 40 kg body weight
1 blue or purple pipette per dog to be split in 3 spots



Dogs over 40 kg body weight
1 red pipette per dog to be split in 4 spots

OR



4b recommendation: Regardless of the dog's body weight, using the applicator tip, part the hair at the base of the tail and begin applying the veterinary medicinal product directly onto the skin in a continuous line from the base of the tail along the centre of the back all the way up to the shoulder blades, as shown in the diagram, squeezing the applicator until it is empty.

Treatment schedule:

Following a single administration, the veterinary medicinal product will prevent infestation for one month. The treatment can be repeated once a month.

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

Apart from erythema and cosmetic hair coat changes at the site of application, no adverse reactions were observed in healthy puppies aged 7 weeks, topically treated 7 times at 2-week intervals and with up to 5 times the highest recommended dose.
After accidental ingestion of the highest recommended dose, vomiting, salivation and diarrhoea may occur, however these should resolve without treatment.

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:

QP53AC54

4.2 Pharmacodynamics

Dinotefuran is an insecticide. Its structure is derived from the neurotransmitter acetylcholine and acts on nicotinic acetylcholine receptors of the insect nerve synapse. Once bound to these receptors, the agonist action of repeated excitatory impulses kills the insect. Insects do not have to ingest dinotefuran, it kills by contact. Dinotefuran has low affinity to mammalian acetylcholine receptor sites.

Pyriproxyfen is a photostable insect growth regulator (IGR). It acts through contact, by mimicking the juvenile hormone, which regulates the moulting of insects from one life stage to the next. Pyriproxyfen stops the flea life cycle by both inducing premature oviposition and also suppressing yolk deposition in flea eggs, leading to the production of infertile eggs. Pyriproxyfen also blocks the development of juvenile stages (larvae and early (pharate) pupae) into adult emergence. This prevents infestation within the environment of the treated animal.

Permethrin is a synthetic pyrethroid. Pyrethroids act as neurotoxins on voltage-gated sodium channels by slowing their activation and inactivation properties. This results in hyperexcitability and death of the parasite. Permethrin is acaricide and insecticide. It also possesses repellent properties.

A synergistic effect was observed *in vitro* when dinotefuran was administered in conjunction with permethrin, leading to a faster onset of insecticidal activity *in vivo*. On the day of first treatment this veterinary medicinal product results in adequate flea adulticidal activity within 12 hours after application.

The anticipated clinical benefit resulting from a combination of dinotefuran with permethrin was demonstrated in one laboratory study on dogs which showed a prolongation of the duration of efficacy against *C. canis* fleas to 4 weeks.

4.3 Pharmacokinetics

Following topical application, dinotefuran and pyriproxyfen are partially absorbed through the dog's skin leading to systemic exposure. For permethrin, the plasma levels remain under the limit of quantification.

The three active substances rapidly distribute over the body surface of the animal within the first day, with maximum concentrations obtained 3 days after the application. The three active substances were still measurable in different zones of the hair coat one month after treatment.

Environmental properties

The veterinary medicinal product is dangerous for fish and other aquatic organisms.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: use immediately.

5.3. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

Spot-on applicator made of a multilayered complex of aluminium and polyethylene (PE) with HDPE, top-sealed with a liner complex (aluminium/polyester/sealable PE layer) in a cardboard box.

Pack sizes:
Cardboard box of 1, 3, 4, 6, 12, 24 or 48 spot-on applicators of 0.8 ml, 1.6 ml, 3.6 ml, 4.7 ml or 8.0 ml. (Only one size per box).

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 it is dangerous for fish and other aquatic organisms. Do not contaminate ponds, waterways or ditches with the veterinary medicinal product or with used containers.
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

Ceva Santé Animale

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/156/001–035

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 04/12/2013

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

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product not subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).