SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantix Spot-on solution for dogs over 10 kg up to 25 kg [AT, CZ, FR, DE, EL, HU, IE, IT, NL, PT, SK, ES, UK]
Bayvantic Vet. Spot-on solution for dogs over 10 kg up to 25 kg [DK, FI, NO]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pipette of 2.5 ml contains:

Active substances:

Imidacloprid: 250.0 mg
Permethrin (40/60): 1250.0 mg

Excipient(s):

N-Methylpyrrolidone: 1210 mg
Butylhydroxytoluene (E321): 2.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on solution
Clear yellowish to brownish solution

4. CLINICAL PARTICULARS

4.1 Target species

Dogs (over 10 kg up to 25 kg)

For dogs less than or equal to 10 kg or more than 25 kg body weight, use the appropriate Advantix Spot-on solution product (see section 4.9).

4.2 Indications for use, specifying the target species

For the treatment and prevention of flea (*Ctenocephalides canis*, *Ctenocephalides felis*) infestation.

Fleas on dogs are killed within one day following treatment. One treatment prevents further flea infestation for four weeks. The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

For the treatment of biting lice (*Trichodectes canis*).

The product has persistent acaricidal and repellent efficacy against tick infestations (*Rhipicephalus sanguineus* and *Ixodes ricinus* for four weeks, and *Dermacentor reticulatus* for three weeks).

By repelling and killing the tick vector *Rhipicephalus sanguineus,* the product reduces the likelihood of transmission of the pathogen *Ehrlichia canis,* thereby reducing the risk of canine ehrlichiosis. The reduction in risk has been shown in studies to commence from 3 days following application of the product and to persist for 4 weeks.

Ticks already on the dog may not be killed within two days after treatment and may remain attached and visible. Therefore the removal of ticks already on the dog at the time of treatment is recommended, in order to prevent them from attaching and having a blood meal.

One treatment provides repellent (anti-feeding) activity against sand flies (*Phlebotomus papatasi* for two weeks and *Phlebotomus perniciosus* for three weeks), against mosquitoes (*Aedes aegypti* for two weeks and *Culex pipiens* for four weeks) and against stable flies (*Stomoxys calcitrans*) for four weeks.

Reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*) for up to 3 weeks. The effect is indirect due to product's activity against the vector.

4.3 Contraindications

In the absence of available data the product should not be used on puppies of less than 7 weeks of age or 10 kg of weight.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Do not use on cats. (Refer to section 4.5 – Special precautions for use).

4.4 Special warnings for each target species

There may be an attachment of single ticks or bites by single sand flies or mosquitoes. For this reason, a transmission of infectious diseases by these parasites cannot be completely excluded if conditions are unfavourable.

It is recommended to apply the treatment at least 3 days before expected exposure to *E. canis*. With regard to *E. canis*, studies have demonstrated a reduced risk of canine ehrlichiosis in dogs exposed to *Rhipicephalus sanguineus* ticks infected with *E. canis* from 3 days following application of the product and to persist for 4 weeks.

Immediate protection against sandflies bites is not documented. Treated dogs for the reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies *P. Perniciosus* should be kept in a protected environment during the first 24 hours after the initial treatment application.

4.5 Special precautions for use

i) Special precautions for use in animals

Care should be taken to avoid the content of the pipette coming into contact with the eyes or mouth of the recipient dogs.

Care should be taken to administer the product correctly as described under section 4.9. In particular oral uptake due to the licking of the application site by treated or in-contact animals should be avoided.

Do not use on cats.

This product is extremely poisonous to cats and could be fatal due to the unique physiology of cats which is unable to metabolise certain compounds including permethrin. To prevent cats from being accidentally exposed to the product, keep treated dogs away from cats after treatment 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 product. Seek veterinary advice immediately if this occurs.

Consult your veterinary surgeon before using the product on sick and debilitated dogs.

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

Avoid contact between the product and skin, eyes or mouth.
Do not eat, drink or smoke during application.
Wash hands thoroughly after use.
In case of accidental spillage onto skin, wash off immediately with soap and water.
People with known skin sensitivity may be particularly sensitive to this product.
The predominant clinical symptoms that in extremely rare case may be shown are transient sensory irritations of the skin like tingling, burning sensation or numbness.
If the product gets accidentally into the eyes, they should be thoroughly flushed with water. If skin or if eye irritation persists obtain medical attention immediately and show the package insert to the physician.
Do not ingest. In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.
Treated dogs should not be handled especially by children until the application site is dry. This may be ensured by treating the dogs e.g. in the evening. Recently treated dogs should not be allowed to sleep together with their owner, especially children.
In order to prevent children from getting access to pipettes, keep the pipette in the original packaging until ready for use and dispose of used pipettes immediately.

Laboratory studies in rabbits and rats with the excipient N-Methylpyrrolidone 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.

iii) Other precautions

As the product is dangerous to aquatic organisms, treated dogs must not under any circumstances be allowed into any type of surface water for at least 48 hours after treatment.

The solvent in Advantix Spot-on solution may stain certain materials including leather, fabrics, plastics and finished surfaces. Allow the application site to dry before permitting contact with such materials.

4.6 Adverse reactions (frequency and seriousness)

Application site itching and hair change (e.g. greasy fur) and vomiting were uncommonly observed in clinical studies. Other reactions like redness, inflammation and hair loss at the application site and diarrhoea were reported rarely.

On very rare occasions reactions in dogs including transient skin sensitivity (scratching and rubbing) or lethargy were reported in spontaneous (pharmacovigilance) reports. These reactions are generally self-resolving.

In very rare cases dogs may show behaviour changes (agitation, restlessness, whining or rolling), gastro-intestinal symptoms (hypersalivation, diminished appetite) and neurological signs such as unsteady movement and twitching in dogs susceptible to the ingredient permethrin. These signs are generally transient and self-resolving.

Poisoning following inadvertent oral uptake in dogs is unlikely but may occur in very rare cases. In this event, neurological signs such as tremor and lethargy can occur. Treatment should be symptomatic. There is no known specific antidote.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

The recommended minimum dose is:
10 mg/kg body weight (bw) imidacloprid and 50 mg/kg body weight (bw) permethrin.

Dosing Scheme for Advantix Spot-on:

Dogs (kg body weight)	**Trade name**	**Volume (ml)**	**Imidacloprid (mg/kg body weight)**	**Permethrin (mg/kg body weight)**
≤ 4 kg	Advantix Spot-on for dogs up to 4 kg	0.4 ml	minimum of 10	minimum of 50
>4 kg ≤ 10 kg	Advantix Spot-on for dogs over 4 kg up to 10 kg	1.0 ml	10 - 25	50 - 125
>10 kg ≤ 25 kg	Advantix Spot-on for dogs over 10 kg up to 25 kg	2.5 ml	10 - 25	50 - 125
>25 kg ≤ 40 kg	Advantix Spot-on for dogs over 25 kg up to 40 kg	4.0 ml	10 - 16	50 - 80

To reduce re-infestation from emergence of new fleas, it is recommended to treat all dogs in a household. Other animals living in the same household should also be treated with a suitable product. To aid further in reducing environmental challenge, the additional use of a suitable environmental treatment against adult fleas and their developmental stages is recommended.

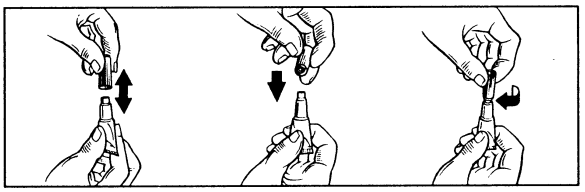
The product remains effective if the animal becomes wet. However, prolonged, intense exposure to water should be avoided. In cases of frequent water exposure the persistent efficacy may be reduced. In these cases do not retreat more frequently than once weekly. If a dog requires a shampoo, it should be administered before applying Advantix or at least 2 weeks after application, to optimise efficacy of the product.

In case of biting louse infestation, a further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

To protect a dog over the whole sand fly season, treatment should be compliantly continued throughout.

For dermal use only. Apply only to undamaged skin.

Remove one pipette from the package. Hold applicator pipette in an upright position, twist and pull cap off. Turn the cap around and place the other end of cap back on pipette. Twist cap to break seal, then remove cap from pipette.

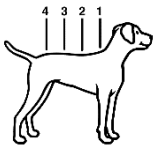


For dogs 10 kg body weight or less:

With the dog standing still, part the coat between the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze firmly several times to empty the contents directly onto the skin.

For dogs of more than 10 kg body weight:

With the dog standing still, the entire contents of the Advantix pipette should be applied evenly to four spots on the top of the back from the shoulder to the base of the tail. At each spot, part the hair until the skin is visible. Place the tip of the pipette on the skin and gently squeeze to expel a portion of the solution on the skin. Do not apply an excessive amount of solution at any one spot that could cause some of the solution to run off the side of the dog.



4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No adverse clinical signs were noted in healthy puppies or adult dogs exposed to 5x overdosage or for puppies whose mothers were treated with 3x overdosage of the product.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antiparasitic agent,
ATC vet code: QP53AC54

Advantix Spot-on is an ectoparasiticide for topical use containing imidacloprid and permethrin. This combination acts as an insecticide, acaricide and as a repellent.

5.1 Pharmacodynamic properties

Imidacloprid is an ectoparasiticide belonging to the chloronicotinyl group of compounds. Chemically, it can be classified as a chloronicotinyl nitroguanidine. Imidacloprid is effective against adult fleas and larval flea stages. In addition to the adulticide flea efficacy of imidacloprid, a larvicidal flea efficacy in the surroundings of the treated pet has been demonstrated. Larval stages in the dog`s immediate surroundings are killed following contact with a treated animal. It has a high affinity for the nicotinergic acetylcholine receptors in the post-synaptic region of the central nervous system (CNS) in insects. The ensuing inhibition of cholinergic transmission in insects results in paralysis and death of the parasite.

Permethrin belongs to the type I class of pyrethroid acaricides and insecticides and also acts as repellent. Pyrethroids affect the voltage-gated sodium channels in vertebrates and non-vertebrates. Pyrethroids are so called "open channel blockers" affecting the sodium channel by slowing both the activation and the inactivation properties thus leading to hyperexcitability and death of the parasite.

In the combination of both substances, it has been shown Imidacloprid functions as the activator of arthropod ganglion and therefore increases the efficacy of permethrin.

The product provides repellent (anti-feeding) activity against ticks, sand flies and mosquitoes, thus preventing the repelled parasites from taking a blood meal and thus reducing the risk of Canine Vector-Borne Disease (CVBD) transmission (e.g. borreliosis, rickettsiosis, ehrlichiosis, leishmaniosis). However, there may be an attachment of single ticks or bites by single sand flies or mosquitoes. For this reason, a transmission of infectious diseases by these parasites cannot be completely excluded if conditions are unfavourable. The product provides repellent (anti-feeding) activity against stable flies thereby assisting in the prevention of fly-bite dermatitis.

The product provides repellent activity (anti-feeding activity) against *Phlebotomus perniciosus* (> 80% for 3 weeks), mosquitoes and ticks. Field data from an endemic area showed that the product indirectly reduces the risk of transmission of *Leishmania infantum* from infected sandflies (*Phlebotomus perniciosus*) for up to 3 weeks, thereby reducing the risk of canine leishmaniosis in treated dogs.

5.2 Pharmacokinetic particulars

The product is indicated for dermal administration. Following topical application in dogs, the solution rapidly distributes over the body surface of the animal. Both active substances remain detectable on the skin and hair of the treated animal for 4 weeks.

Acute dermal studies in the rat and target animal, overdose and serum kinetic studies have established that systemic absorption of both active substances after application on intact skin is low, transient and not relevant for the clinical efficacy.

5.3 Environmental properties

The product should not be allowed to enter water courses as this may be dangerous for fish and aquatic organisms. For treated dogs, please see section 4.5.

Permethrin containing products are toxic to honey bees.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321)
N-Methylpyrrolidone
Miglyol 812
Citric acid (E330)

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf-life of product in foil pouch:	5 years.
Shelf life of product after opening foil pouch:	2 years (all pipettes should be used within 2 years after opening the foil pouch or before expiry date on the pipette whichever is shorter).
Shelf-life of the broached pipette:	Not applicable, once opened, the entire content of the pipette has to be applied to the animal's skin.

6.4. Special precautions for storage

Do not freeze.
After opening the foil pouch store in a dry place at a temperature not above 30°C.

6.5 Nature and composition of immediate packaging

Fill volume:	2.5 ml clear yellowish to brownish, non-aqueous solution per 2.5 ml pipette (250 mg imidacloprid, 1250 mg permethrin).
Type of the container:	White polypropylene pipette. White polypropylene cap.
Material of the secondary packaging:	Polychlorotrifluoroethylene PCTFE/PVC heat sealed blister packs in one or more aluminium pouch(es) and a cardboard box.
Package sizes:	Packs containing 1, 2, 3, 4, 6 and 24 unit dose pipettes. 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

After use, replace cap on tube. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[to be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[to be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[to be completed in accordance with national requirements after conclusion of the MR phase]

10. DATE OF REVISION OF THE TEXT

[to be completed in accordance with national requirements after conclusion of the MR phase]

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Outer carton, pack size of 1, 2, 3, 4, 6 and 24 pipettes

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantix® Spot-on solution for dogs over 10 kg up to 25 kg [AT, CZ, FR, DE, EL, HU, IE, IT, NL, PT, SK, ES, UK]

Bayvantic vet® Spot-on solution for dogs over 10 kg up to 25 kg[DK, FI, NO]

2. STATEMENT OF ACTIVE SUBSTANCES

Each 2.5 ml pipette contains:
Active substances: 250 mg imidacloprid, 1250 mg permethrin

3. PHARMACEUTICAL FORM

Spot-on solution

4. PACKAGE SIZE

1 pipette (1x 2.5 ml)
2 pipettes (2x 2.5 ml)
3 pipettes (3x 2.5 ml)
4 pipettes (4x 2.5 ml)
6 pipettes (6x 2.5 ml)
24 pipettes (24x 2.5 ml)

5. TARGET SPECIES

Dogs

6. INDICATION(S)

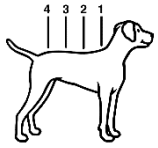
[For cartons: this text for front (only) of carton.]
- Eliminates ticks, fleas and biting lice
- Repels ticks, mosquitos, sand flies, and stable flies
- Reduces the risk of transmission of canine leishmaniosis and canine ehrlichiosis

[For cartons: this text for back (only) of carton]
- Eliminates fleas (treatment and prevention); can be used as a part of the strategy of treatment of flea allergic dermatitis (FAD).
- Eliminates biting lice.
- Repels and eliminates ticks; reducing the risk of transmission of CVBD (diseases such as borreliosis, rickettsiosis, and ehrlichiosis).
- Repels mosquitoes and sand flies; reducing the risk of transmission of leishmaniosis.
- Repels stable flies; contributing to the prevention of fly-bite dermatitis.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For external use only.
Read the package leaflet before use.
Keep the foil pouch with the blisters in the outer carton.

[Dog Application –Pictogram (size specific corresponding to the product size]



8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
Do not use on puppies of less than 7 weeks of age or 10 kg of weight.
Do not use on cats.

[Do Not Use on Cats -Pictogram]

10. EXPIRY DATE

Expiry/EXP {month/year}
[Internal comment for translation: Please use your full national term for "Expiry" and the English short term "EXP"; this is to bridge to the pouch, blister foil and pipette label, where only the term "EXP" is used.]

Use within 24 months after opening the foil pouch or before EXP, whichever is shorter.

11. SPECIAL STORAGE CONDITIONS

Do not freeze.
After opening the foil pouch store in a dry place at a temperature not above 30°C.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
[Prescription status to be completed nationally]

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[to be completed nationally]

Manufactured by
KVP Pharma + Veterinär Produkte GmbH
Projensdorfer Str. 324, 24106 Kiel
Germany

16. MARKETING AUTHORISATION NUMBER(S)

[to be completed nationally]

17. MANUFACTURER'S BATCH NUMBER

Batch No./Lot {number}
[Internal comment for translation: Please use your full national term for "Batch No." and the English short term "Lot"; this is to bridge to the pouch, blister foil and pipette label, where only the term "Lot" is used.]

 Tick  Flea  Mosquito  Sandfly  Stable Fly  Lice 
Leishmaniosis

[Note: Depending on prevalent pests in CMSs, not all target pest pictograms may be used in every country]

[Figure of pipette, photo of dog, Elanco Logo]

Other Information:

- Remains effective if the dog becomes wet.
- Provides a larvicidal effect against fleas in the immediate surroundings of the treated dogs
- Can be used on both pregnant and lactating bitches.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pipette label – international version (no translation required)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantix® [AT, CZ, FR, DE, EL, HU, IE, IT, NL, PT, SK, ES, UK]

Bayvantic vet® [DK, FI, NO]

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

100 mg/ml imidacloprid(e)
500 mg/ml permethrin(e)

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

2.5 ml

4. ROUTE(S) OF ADMINISTRATION

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

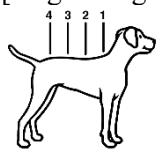
Lot {number}
[Internal comment: Do not translate "Lot"]

7. EXPIRY DATE

EXP {month/year}
[Internal comment: Do not translate "EXP"]

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

[Dog-Pictogram – Size specific corresponding to the product size]



> 10 kg ≤ 25 kg

[Do Not Use on Cats -Pictogram]

Elanco Logo

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister – international version (no translation required)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantix® [AT, CZ, FR, DE, EL, HU, IE, IT, NL, PT, SK, ES, UK]

Bayvantic vet® [DK, FI, NO]

2. NAME OF THE MARKETING AUTHORISATION HOLDER

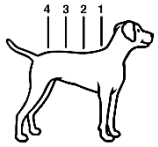
Elanco Logo

3. EXPIRY DATE

4. BATCH NUMBER

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

[Dog-Pictogram – Size specific corresponding to the product size – to be printed in black and white]



> 10 kg ≤ 25 kg
2.5 ml
[Tube-picto]

[Do Not Use on Cats -Pictogram]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Foil pouch – international version (no further translation required)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantix® [AT, CZ, FR, DE, EL, HU, IE, IT, NL, PT, SK, ES, UK]

Bayvantic vet® [DK, FI, NO]

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco Logo

3. EXPIRY DATE

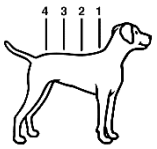
EXP {month/year}

4. BATCH NUMBER

Lot {number}

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

[Dog-Pictogram – Size specific corresponding to the product size – to be printed in black and white]



> 10 kg ≤ 25 kg
2.5 ml

[Tube-picto]

FURTHER INFORMATION

[Do Not Use on Cats -Pictogram]

Country code	
IE/UK	Use within 24 months after opening the foil pouch or before EXP, whichever is shorter.
CZ	Po otevření vnějšího aluminiového obalu použijte do 24 měsíců nebo před uplynutím doby použitelnosti EXP, cokoli je kratší.

DK	Anvendes inden for 24 måneder efter åbningen af folieposen eller inden EXP alt efter hvad der kommer først.
AT/BE/DE/LU	Innerhalb von 24 Monaten nach Öffnen des Aluminiumbeutels oder vor EXP verwenden, was auch immer kürzer ist.
GR	Να χρησιμοποιείται εντός 24 μηνών μετά το άνοιγμα του περιτυλίγματος ή πριν από την ημερομηνία EXP -οποιαδήποτε από τις δύο προηγείται.
ES	Utilizar en el plazo de 24 meses una vez abierta la bolsa de aluminio, siempre que ese periodo no supere la EXP.
FI	Käytä 24 kuukauden kuluessa alumiinipussin avaamisesta ja joka tapauksessa ennen EXP-päivämäärää.
FI	Använd inom 24 månader efter det att foliepåsen öppnats eller före EXP om det är kortare.
BE/FR/LU	A utiliser dans les 24 mois après ouverture du sachet aluminium, ou avant EXP si celle-ci est plus courte.
HU	Felhasználható a lejárati időn belül (EXP:), vagy a tasak kibontását követően maximum 24 hónapig.
IT	Utilizzare entro 24 mesi dopo l'apertura della busta di alluminio o prima della data di scadenza (EXP) qualora sia più breve.
BE/NL	Gebruiken binnen 24 maanden na opening van het zakje of vóór EXP, het kortste van de twee.
NO	Brukes innen 24 måneder etter åpning av folieposen eller før EXP, avhengig av hva som kommer først.
PT	Aplicar no prazo de 24 meses após abertura da saqueta de alumínio ou antes de EXP, caso seja mais curto.
SK	Použite do 24 mesiacov po otvorení vonkajšieho alumíniového obalu alebo pred uplynutím EXP, podľa toho čo nastane skôr.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

Advantix® Spot-on solution for Dogs

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder
[to be completed nationally]

Manufacturer responsible for batch release
KVP Pharma + Veterinär Produkte GmbH
Projensdorfer Str. 324, 24106 Kiel
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantix® Spot-on solution for dogs up to 4 kg Advantix® Spot-on solution for dogs over 4 kg up to 10 kg Advantix® Spot-on solution for dogs over 10 kg up to 25 kg Advantix® Spot-on solution for dogs over 25 kg up to 40 kg	[AT, CZ, FR, DE, EL, HU, IE, IT, NL, PT, SK, ES, UK]
Advantix® Spot-on solution for dogs over 40 kg up to 60 kg	[AT, CZ, DE, EL, HU, IE, IT, NL, PT, SK, ES, UK]
ADVANTIX TRES GRAND CHIEN	[FR]
Bayvantic vet® Spot-on solution for dogs up to 4 kg Bayvantic vet® Spot-on solution for dogs over 4 kg up to 10 kg Bayvantic vet® Spot-on solution for dogs over 10 kg up to 25 kg Bayvantic vet® Spot-on solution for dogs over 25 kg up to 40 kg Bayvantic vet® Spot-on solution for dogs over 40 kg up to 60 kg	[DK, FI, NO]

imidacloprid, permethrin

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each pipette contains:

	Pipette	Imidacloprid	Permethrin	N-Methylpyrrolidone	Butylhydroxytoluene (E321)
Advantix® Spot-on solution for dogs ≤ 4 kg	0.4 ml	40 mg	200 mg	194 mg	0.4 mg
Advantix® Spot-on solution for dogs > 4 ≤ 10 kg	1.0 ml	100 mg	500 mg	484 mg	1.0 mg
Advantix® Spot-on solution for dogs > 10 ≤ 25 kg	2.5 ml	250 mg	1250 mg	1210 mg	2.5 mg
Advantix® Spot-on solution for dogs > 25 kg ≤ 40 kg	4.0 ml	400 mg	2000 mg	1936 mg	4.0 mg
Advantix® Spot-on solution for dogs >40kg ≤ 60kg	6.0 ml	600 mg	3000 mg	2904 mg	6.0 mg

For dogs > 60 kg the appropriate combination with other sized pipettes should be used.

A clear yellowish to brownish spot-on solution.

4. INDICATIONS

For the treatment and prevention of flea (*C. canis*, *C. felis*) infestation and for the treatment of biting lice (*Trichodectes canis*) on dogs.

Fleas on dogs are killed within one day following treatment. One treatment prevents further flea infestation for four weeks. The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

The product has persistent acaricidal and repellent efficacy against tick infestations (*Rhipicephalus sanguineus* and *Ixodes ricinus* for four weeks, and *Dermacentor reticulatus* for three weeks).

By repelling and killing the tick vector *Rhipicephalus sanguineus,* the product reduces the likelihood of transmission of the pathogen *Ehrlichia canis,* thereby reducing the risk of canine ehrlichiosis. The reduction in risk has been shown in studies to commence from 3 days following application of the product and to persist for 4 weeks.

Ticks already on the dog may not be killed within two days after treatment and may remain attached and visible. Therefore the removal of ticks already on the dog at the time of treatment is recommended, in order to prevent them from attaching and having a blood meal.

One treatment provides repellent (anti-feeding) activity against sand flies (*P. papatasi* for two weeks and *Phlebotomus perniciosus* for three weeks), against mosquitoes (*A. aegypti* for two weeks and *C. pipiens* for four weeks) and against stable flies (*S. calcitrans*) for four weeks.

Reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*) for up to 3 weeks. The effect is indirect due to product's activity against the vector.

Sand flies	*P. perniciosus*	3 weeks
	P. papatasi	2 weeks
Mosquitoes	*A. aegypti*	2 weeks

	C. pipiens	4 weeks
Stable flies	*S. calcitrans*	4 weeks

5. CONTRAINDICATIONS

In the absence of available data the product should not be used on puppies of less than 7 weeks of age or 1.5 kg of weight. According to the dog's body weight the corresponding Advantix® product must be used, see dosing scheme.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Do not use on cats.

6. ADVERSE REACTIONS

Application site itching and hair change (e.g. greasy fur) and vomiting were uncommonly observed in clinical studies. Other reactions like redness, inflammation and hair loss at the application site and diarrhoea were reported rarely.

On very rare occasions reactions in dogs including transient skin sensitivity (scratching and rubbing) or lethargy were reported in spontaneous (pharmacovigilance) reports. These reactions are generally self-resolving.

In very rare cases dogs may show behaviour changes (agitation, restlessness, whining or rolling), gastro-intestinal symptoms (hypersalivation, diminished appetite) and neurological signs such as unsteady movement and twitching in dogs susceptible to the ingredient permethrin. These signs are generally transient and self-resolving.

Poisoning following inadvertent oral uptake in dogs is unlikely but may occur in very rare cases. In this event, neurological signs such as tremor and lethargy can occur. Treatment should be symptomatic. There is no known specific antidote.

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

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

The recommended minimum dose is:
10 mg/kg body weight (bw) imidacloprid and 50 mg/kg body weight (bw) permethrin.

Dosing Scheme

Dogs (kg bw)	**Trade name**	**Volume (ml)**	**Imidacloprid (mg/kg bw)**	**Permethrin (mg/kg bw)**

4 kg and less	Advantix® Spot-on for dogs up to 4 kg	0.4 ml	minimum of 10	minimum of 50
More than 4 to 10 kg	Advantix® Spot-on for dogs over 4 kg up to 10 kg	1.0 ml	10 - 25	50 - 125
More than 10 to 25 kg	Advantix® Spot-on for dogs over 10 kg up to 25 kg	2.5 ml	10 - 25	50 - 125
More than 25 to 40 kg	Advantix® Spot-on for dogs over 25 kg up to 40 kg	4.0 ml	10 - 16	50 - 80

To reduce re-infestation from emergence of new fleas, it is recommended to treat all dogs in a household. Other animals living in the same household should also be treated with a suitable product. To aid further in reducing environmental challenge, the additional use of a suitable environmental treatment against adult fleas and their developmental stages is recommended.

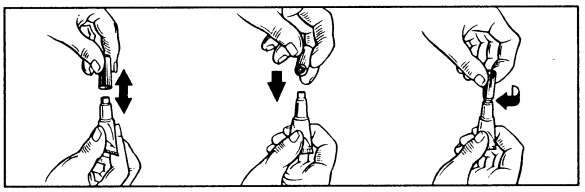
The product remains effective if the animal becomes wet. However, prolonged, intense exposure to water should be avoided. In cases of frequent water exposure the persistent efficacy may be reduced. In these cases do not retreat more frequently than once weekly. If a dog requires a shampoo, it should be administered before applying Advantix® or at least 2 weeks after application, to optimise efficacy of the product.

In case of biting louse infestation, a further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

To protect a dog over the whole sand fly season, treatment should be compliantly continued throughout.

Method of Administration

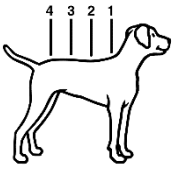
Remove one pipette from the package. Hold applicator pipette in an upright position, twist and pull cap off. Turn the cap around and place the other end of cap back on pipette. Twist cap to break seal, then remove cap from pipette.



<u>For dogs up to 10 kg body weight:</u>
With the dog standing still, part the coat between the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze firmly several times to empty the contents directly onto the skin.

<u>For dogs over 10 kg body weight:</u>

With the dog standing still, the entire contents of the Advantix® pipette should be applied evenly to four spots on the top of the back from the shoulder to the base of the tail. At each spot, part the hair until the skin is visible. Place the tip of the pipette on the skin and gently squeeze to expel a portion of the solution on the skin



9. ADVICE ON CORRECT ADMINISTRATION

For external use only.
Apply only to undamaged skin.
Do not apply an excessive amount of solution at any one spot that could cause some of the solution to run off the side of the dog.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not freeze.
After opening the foil pouch store in a dry place at a temperature not above 30°C.
For 0.4 ml – 4.0 ml: Use within 24 months after opening the foil pouch or before EXP, whichever is shorter.
For 6.0 ml: Use within 12 months after opening the foil pouch or before EXP, whichever is shorter.

Do not use this veterinary medicinal product after the expiry date which is stated on the pipette, foil pouch, or carton after EXP. The expiry date refers to the last day of that month.

12. SPECIAL WARNINGS

Special warnings for each target species:

There may be an attachment of single ticks or bites by single sand flies or mosquitoes. For this reason, a transmission of infectious diseases by these parasites cannot be completely excluded if conditions are unfavourable. However, the product provides repellent (anti-feeding) activity against ticks, sand flies and mosquitoes, thus preventing the repelled parasites from taking a blood meal and thus reducing the risk of Canine Vector-Borne Disease (CVBD) transmission (diseases such as borreliosis, rickettsiosis, ehrlichiosis, leishmaniosis).

Immediate protection against sandflies bites is not documented. Treated dogs for the reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies *P. Perniciosus* should be kept in a protected environment during the first 24 hours after the initial treatment application.

It is recommended to apply the treatment at least 3 days before expected exposure to *E. canis*. With regard to *E. canis*, studies have demonstrated a reduced risk of canine ehrlichiosis in dogs exposed to *Rhipicephalus sanguineus* ticks infected with *E. canis* from 3 days following application of the product and to persist for 4 weeks.

Special precautions for use in animals:

Care should be taken to avoid the content of the pipette coming into contact with the eyes or mouth of the recipient dogs.

Care should be taken to administer the product correctly as described under *Method of Administration.* In particular oral uptake due to the licking of the application site by treated or in-contact animals should be avoided.

Do not use on cats.

This product is extremely poisonous to cats and could be fatal due to the unique physiology of cats which is unable to metabolise certain compounds including permethrin. To prevent cats from being accidentally exposed to the product, keep treated dogs away from cats after treatment 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 product. Seek veterinary advice immediately if this occurs.

Consult your veterinary surgeon before using the product on sick and debilitated dogs.

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

Avoid contact between the product and skin, eyes or mouth.
Do not eat, drink or smoke during application.
Wash hands thoroughly after use.
In case of accidental spillage onto skin, wash off immediately with soap and water.
People with known skin sensitivity may be particularly sensitive to this product.
The predominant clinical symptoms that in extremely rare case may be shown are transient sensory irritations of the skin like tingling, burning sensation or numbness.
If the product gets accidentally into the eyes, they should be thoroughly flushed with water. If skin or if eye irritation persists obtain medical attention immediately and show the package insert to the physician.
Do not ingest. In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.
Treated dogs should not be handled especially by children until the application site is dry. This may be ensured by treating the dogs e.g. in the evening. Recently treated dogs should not be allowed to sleep together with their owner, especially children.
In order to prevent children from getting access to pipettes, keep the pipette in the original packaging until ready for use and dispose of used pipettes immediately.

The warning below only applies to products for dogs of more than 10 kg:
Laboratory studies in rabbits and rats with the excipient N-Methylpyrrolidone 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.

Other precautions:

As the product is dangerous to aquatic organisms, treated dogs must not under any circumstances be allowed into any type of surface water for at least 48 hours after treatment.

The solvent in Advantix® Spot-on solution may stain certain materials including leather, fabrics, plastics and finished surfaces. Allow the application site to dry before permitting contact with such materials.

Pregnancy and lactation:

The product can be used during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:

None known.

Overdose (symptoms, emergency procedures, antidotes):

No adverse clinical signs were noted in healthy puppies or adult dogs exposed to 5x overdosage or for puppies whose mothers were treated with 3x overdosage of the product.

Incompatibilities:

None known.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

After use, replace cap on tube. Medicines should not be disposed of via wastewater. Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Advantix® Spot-on is an ectoparasiticide for topical use containing imidacloprid and permethrin. This combination acts as an insecticide, acaricide and as a repellent.

Imidacloprid is effective against adult fleas and larval flea stages. In addition to the adulticide flea efficacy of imidacloprid, a larvicidal flea efficacy in the surroundings of the treated pet has been demonstrated. Larval stages in the dog`s immediate surroundings are killed following contact with a treated animal.

Permethrin containing products are toxic to honey bees.

Pack sizes: 0.4 ml, 1.0 ml, 2.5 ml, 4.0 ml and 6.0 ml per pipette; packs containing 1, 2, 3, 4, 6 and 24 single-use pipette packs.
Not all pack sizes may be marketed.

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