

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard 11 mg chewable tablets for dogs 2-4 kg
NexGard 28 mg chewable tablets for dogs > 4-10 kg
NexGard 68 mg chewable tablets for dogs > 10-25 kg
NexGard 136 mg chewable tablets for dogs > 25-50 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each chewable tablet contains:

| NexGard | Afoxolaner (mg) |
|--------------------------------------|-----------------|
| chewable tablets for dogs 2-4 kg | 11.3 |
| chewable tablets for dogs > 4-10 kg | 28.3 |
| chewable tablets for dogs > 10-25 kg | 68.0 |
| chewable tablets for dogs > 25-50 kg | 136.0 |

Excipient:

Potassium sorbate (E202): 3 mg/g.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablets.

Mottled red to reddish brown, circular shaped (tablets for dogs 2-4 kg) or rectangular shaped (tablets for dogs > 4-10 kg, tablets for dogs > 10-25 kg and tablets for dogs > 25-50 kg).

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

Treatment of flea infestation in dogs (*Ctenocephalides felis* and *C. canis*) for at least 5 weeks. The product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

Treatment of tick infestation in dogs (*Dermacentor reticulatus*, *Ixodes ricinus*, *Rhipicephalus sanguineus*). One treatment kills ticks for up to one month.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance. For fleas (*C. felis*), the onset of effect is within 8 hours of attachment. For ticks, the onset of effect (death) is within 48 hours of attachment.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

Parasites need to start feeding on the host to become exposed to afoxolaner; therefore the risk of the transmission of parasite borne diseases cannot be excluded.

4.5 Special precautions for use

Special precautions for use in animals

In the absence of available data, treatment of puppies less than 8 weeks of age and/or dogs less than 2 kg bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

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

To prevent children from getting access to the veterinary medicinal product, remove only one chewable tablet at a time from the blister. Return the blister with the remaining chewable tablets into the carton.

Wash hands after handling the product.

4.6 Adverse reactions (frequency and seriousness)

None.

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic effects, or any adverse effect on the reproductive capacity of males and females.

The safety of the veterinary medicinal product has not been established during pregnancy and lactation or in breeding dogs. Use only accordingly to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

For oral use.

Dosage:

The product should be administered at a dose of 2.7-6.9 mg/kg bodyweight in accordance with the following table:

| Bodyweight of dog (kg) | Strength and number of chewable tablets to be administered | | | |
|------------------------|--|---------------|---------------|----------------|
| | NexGard 11 mg | NexGard 28 mg | NexGard 68 mg | NexGard 136 mg |
| 2-4 | 1 | | | |
| > 4-10 | | 1 | | |
| > 10-25 | | | 1 | |
| > 25-50 | | | | 1 |

For dogs above 50 kg bodyweight, use an appropriate combination of chewable tablets of different/same strengths. The tablets should not be divided.

Method of administration:

The tablets are chewable and palatable to most dogs. If the dog does not accept the tablets directly they may be administered with food.

Treatment schedule:

Monthly intervals throughout the flea and/or tick seasons, based on local epidemiological situations.

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

No adverse reactions were observed in healthy Beagle puppies over 8 weeks of age when treated with 5 times the maximum dose repeated 6 times at intervals of two to four weeks. Diarrhoea and vomiting was observed at approximately 5x overdose (25 mg/kg bodyweight) in Collies.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use.

ATCvet code: QP53BX04.

5.1 Pharmacodynamic properties

Afoxolaner is an insecticide and acaricide belonging to the isoxazoline family. Afoxolaner acts at ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA), thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. This results in uncontrolled activity of the central nervous system and death of insects or acarines. The selective toxicity of afoxolaner between insect/acarines and mammals may be inferred by the differential sensitivity of the insect/acarines' GABA receptors versus mammalian receptors.

Afoxolaner is active against adult fleas as well as several tick species such as *Dermacentor reticulatus* and *D. variabilis*, *Ixodes ricinus* and *I. scapularis*, *Rhipicephalus sanguineus*, *Amblyomma americanum* and *Haemaphysalis longicornis*.

The product kills fleas before egg production and therefore prevents household contamination.

5.2 Pharmacokinetic particulars

After oral administration in dogs, afoxolaner was shown to have high systemic absorption following administration. The absolute bioavailability was 74 %. The mean maximum concentration (C_{max}) was $1,655 \pm 332$ ng/ml in plasma at 2-4 hours (T_{max}) after a 2.5 mg/kg afoxolaner dose.

Afoxolaner distributes into tissues with a volume of distribution of 2.6 ± 0.6 l/kg and a systemic clearance value of 5.0 ± 1.2 ml/hr/kg. The terminal plasma half-life is approximately 2 weeks in dogs; however, half-life of afoxolaner can differ between breeds (e.g. $t_{1/2}$ in Collies at 25 mg/kg bodyweight is up to 47.7 days).

Afoxolaner in the dog is metabolized to more hydrophilic compounds and then eliminated. The metabolites and parent are eliminated from the body via urinary and biliary excretion with the majority eliminated in the bile. No evidence of enterohepatic recycling has been observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch

Soy protein fines

Beef braised flavouring
Povidone (E1201)
Macrogol 400
Macrogol 4000
Macrogol 15 hydroxystearate
Glycerol (E422)
Triglycerides medium-chain
Potassium sorbate (E202)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

The veterinary medicinal product is individually packaged in thermoformed laminated PVC blisters with paper-backed aluminium (Aclar/PVC/Alu).

One carton contains one blister of 1, 3 or 6 chewable tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste material derived from it should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MERIAL
29, avenue Tony Garnier
69007 Lyon
FRANCE

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/159/001-012

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

10 DATE OF REVISION OF THE TEXT

{DD/MM/YYYY}

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu>).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

- A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. STATEMENT OF THE MRLs**
- D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

MERIAL,
4 Chemin du Calquet,
31300 Toulouse,
FRANCE.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

▪ **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

The MAH shall complete, within the stated timeframe, the following measures:

| Description | Due date |
|---|-----------------|
| Quality aspects: Appropriate data shall be provided to demonstrate the need for a preservative in the final formulation. Should the data support removal of the preservative from the formulation an appropriate variation should be submitted. | 2Q 2014 |

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard 11 mg chewable tablets for dogs 2-4 kg
NexGard 28 mg chewable tablets for dogs >4-10 kg
NexGard 68 mg chewable tablets for dogs >10-25 kg
NexGard 136 mg chewable tablets for dogs >25-50 kg

Afoxolaner

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Afoxolaner 11.3 mg
Afoxolaner 28.3 mg
Afoxolaner 68 mg
Afoxolaner 136 mg

3. PHARMACEUTICAL FORM

Chewable tablets

4. PACKAGE SIZE

1 tablet
3 tablets
6 tablets

5. TARGET SPECIES

Dogs 2-4 kg
Dogs > 4-10 kg
Dogs > 10-25 kg
Dogs > 25-50 kg

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Read the package leaflet before use.

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. To be supplied only on veterinary prescription.

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

MERIAL
29, avenue Tony Garnier
69007 Lyon
FRANCE

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/159/001
EU/2/13/159/002
EU/2/13/159/003
EU/2/13/159/004
EU/2/13/159/005
EU/2/13/159/006
EU/2/13/159/007
EU/2/13/159/008
EU/2/13/159/009
EU/2/13/159/010
EU/2/13/159/011
EU/2/13/159/012

17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard 11 mg dogs 2-4 kg
NexGard 28 mg dogs > 4-10 kg
NexGard 68 mg dogs > 10-25 kg
NexGard 136 mg dogs > 25-50 kg

Afoxolaner

2. NAME OF THE MARKETING AUTHORISATION HOLDER

MERIAL

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

NexGard 11 mg chewable tablets for dogs 2-4 kg
NexGard 28 mg chewable tablets for dogs > 4-10 kg
NexGard 68 mg chewable tablets for dogs > 10-25 kg
NexGard 136 mg chewable tablets for dogs > 25-50 kg

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

Marketing authorisation holder:

MERIAL
29, avenue Tony Garnier
69007 Lyon
FRANCE.

Manufacturer responsible for batch release:

MERIAL,
4 Chemin du Calquet,
31300 Toulouse,
FRANCE.

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard 11 mg chewable tablets for dogs (2-4 kg)
NexGard 28 mg chewable tablets for dogs (> 4-10 kg)
NexGard 68 mg chewable tablets for dogs (> 10-25 kg)
NexGard 136 mg chewable tablets for dogs (> 25-50 kg)

Afoxolaner

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

Each chewable tablet contains:

| NexGard | Afoxolaner (mg) |
|-------------------------------------|-----------------|
| chewable tablets for dogs 2-4 kg | 11.3 |
| chewable tablets for dogs >4-10 kg | 28.3 |
| chewable tablets for dogs >10-25 kg | 68.0 |
| chewable tablets for dogs >25-50 kg | 136.0 |

Excipient:

Potassium sorbate (E202): 3 mg/g.

Mottled red to reddish brown, circular shaped (tablets for dogs 2-4 kg), or rectangular shaped (tablets for dogs > 4-10 kg, tablets for dogs > 10-25 kg and tablets for dogs > 25-50 kg).

4. INDICATIONS

Treatment of flea infestation in dogs (*Ctenocephalides felis* and *C. canis*) for at least 5 weeks. The product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

Treatment of tick infestation in dogs (*Dermacentor reticulatus*, *Ixodes ricinus*, *Rhipicephalus sanguineus*). One treatment kills ticks for up to one month.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance. For fleas (*C. felis*), the onset of effect is within 8 hours of attachment. For ticks, the onset of effect (death) is within 48 hours of attachment.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

None.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

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

For oral use

Dosage:

The product should be administered in accordance with the following table to ensure a dose of 2.7-6.9 mg/kg bodyweight.

| Bodyweight of dog (kg) | Strength and number of chewable tablets to be administered | | | |
|------------------------|--|---------------|---------------|----------------|
| | NexGard 11 mg | NexGard 28 mg | NexGard 68 mg | NexGard 136 mg |
| 2-4 | 1 | | | |
| > 4-10 | | 1 | | |
| > 10-25 | | | 1 | |
| > 25-50 | | | | 1 |

For dogs above 50 kg bodyweight, use an appropriate combination of chewable tablets of different/same strengths.

The tablets should not be divided.

Treatment schedule:

Monthly intervals throughout the flea and/or tick seasons, based on local epidemiological situations.

9. ADVICE ON CORRECT ADMINISTRATION

NexGard tablets are chewable and palatable to most dogs. If the dog does not accept the tablets directly they may be administered with food.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not use after the expiry date which is stated on the carton after EXP.

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

12. SPECIAL WARNINGS

Special warnings for each target species:

Parasites need to start feeding on the host to become exposed to afoxolaner; therefore the risk of the transmission of parasite borne diseases cannot be excluded.

Special precautions for use in animals:

In the absence of available data, treatment of puppies less than 8 weeks of age and/or dogs less than 2 kg bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

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

To prevent children from getting access to the veterinary medicinal product, remove only one chewable tablet at a time from the blister. Return the blister with the remaining chewable tablets into the carton.

Wash hands after handling the product.

Pregnancy and lactation:

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic effects, or any adverse effect on the reproductive capacity of males and females. The safety of the veterinary medicinal product has not been established during pregnancy and lactation or in breeding dogs. Use only accordingly to the benefit-risk assessment by the responsible veterinarian.

Overdose (symptoms, emergency procedures, antidotes):

No adverse reactions were observed in healthy Beagle puppies over 8 weeks of age when treated with 5 times the maximum dose repeated 6 times at intervals of 2-4 weeks. Diarrhoea and vomiting was observed at approximately 5x overdose (25 mg/kg bodyweight) in Collies.

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

Ask your veterinary surgeon 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

Detailed information on this product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

15. OTHER INFORMATION

Afoxolaner is an insecticide and acaricide belonging to the isoxazoline family.

NexGard is active against adult fleas as well as several tick species such as *Dermacentor reticulatus* and *D. variabilis*, *Ixodes ricinus* and *I. scapularis*, *Rhipicephalus sanguineus*, *Amblyomma americanum*, and *Haemaphysalis longicornis*.

The product kills fleas before egg production and therefore prevents household contamination.

For each strength, the chewable tablets are available in the following pack sizes:

Carton with 1 blister of 1, 3 or 6 chewable tablets.

Not all pack sizes may be marketed.