[Version 8.1,01/2017]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

K1 KEYVIT 50 mg tablets for dogs (BE, FR, EL, ES, IT, LT, LV, NL, PT, RO)
Vitamin K1 KEYVIT 50 mg tablets for dogs (PL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Phytomenadione, racemic (Vitamin K1) ……. 50.0 mg

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
Round, slight yellow quadrisect tablet with 2 crossing scored lines.
The tablet can be divided into halves and quarters.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

In dogs: treatment of anticoagulant poisoning, following parenteral treatment.

4.3 Contraindications

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

4.4 Special warnings for each target species

As the anticoagulant effects of rodenticides are known to be long lasting it is recommended to administer vitamin K1 with an oral formulation for 3 weeks. The coagulation status (via one stage prothrombin times) has to be evaluated 48 hours after the last administration. If it is prolonged, the treatment is maintained until the clotting time is normal 48 hours after cessation of treatment to avoid relapse. The duration of treatment can be extended as long as the anticoagulant persists in the body.

4.5 Special precautions for use

Special precautions for use in animals

The tablets are flavored. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

The formation of prothrombin may be inadequate when dealing with patients with severe liver dysfunction. Therefore, in these animals, careful monitoring of coagulation parameters after administration of the product is required.

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

People with known hypersensitivity to phytomenadione and/or to any other ingredients of the product should avoid contact with the veterinary medicinal product.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Very rarely, vomiting and skin disorders, as erythema and dermatitis, or allergic edema have been reported.

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

The safety of the veterinary medicinal product has not been established in bitches during pregnancy and lactation. Studies conducted in laboratory animals have shown no teratogenic or foetotoxic effects. Vitamin K1 crosses the placental barrier. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Salicylates (NSAID) and cephalosporins presenting the N-methyl-thiotetrazole moiety may reduce the effect of phytomenadione (vitamin K1), by inhibition of the vitamin K1 recycling.

4.9 Amounts to be administered and administration route

For oral use.
5 mg phytomenadione per kg bodyweight per day, corresponding to 1 tablet per 10 kg bodyweight per day, once a day, for 21 days, in accordance with the following table:

Bodyweight (kg)	**Number of tablets**
< 2.5	*¼ tablet*
from 2.5 to 5	*½ tablet*
> 5 to 7.5	*¾ tablet*
*> 7.5 to 10**	*1 tablet*

** Dog > 10 kg: ¼ tablet per 2.5 kg*

Preferably use in non-fasted animals.
Oral treatment should be undertaken within 12 hours after the end of the emergency treatment by the intravenous route (2 intravenous injections of 5 mg phytomenadione (vitamin K1) per kg bodyweight given 12 hours apart). See section 4.4.

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

No signs of intolerance were displayed at 3 times the therapeutic dose, administered for 3 weeks.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antihaemorrhagic
ATC-vet code: QB02BA01

5.1 Pharmacodynamic properties

Phytomenadione (vitamin K1) is a cofactor necessary for the synthesis of K-dependent coagulation factors (factors II, VII, IX and X). During this synthesis, vitamin K1 is converted into vitamin K1 hydroquinone (active form of vitamin K1) and then into vitamin K1 epoxide. It is then recycled back into vitamin K1. Antivitamin K rodenticides inhibit the recycling of vitamin K1 epoxide, causing a risk of uncontrolled bleeding through the absence of functional factors II, VII, IX and X synthesis. The supply of vitamin K1 must be sufficiently large to activate the alternative hydrogenase enzyme pathway that converts it to its active (hydroquinone) form.

5.2 Pharmacokinetic particulars

After oral administration, phytomenadione (vitamin K1) is rapidly absorbed in the dog.
Some of the vitamin K1 is excreted with the bile in the intestinal tract after metabolism in the liver, and some is excreted in urine (in the form of glucuronoconjugated metabolites).
After administration of a single tablet to dogs (dose rate 5 mg/kg bodyweight) a C_{max} of 1476.8 ng/mL was observed at 1.7 h (T_{max}). The terminal half-life was 6.5 ± 2.0 h (harmonic mean: 6 h).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica, colloidal anhydrous
Calcium hydrogen phosphate dihydrate
Magnesium stearate
Lactose monohydrate
Croscarmellose sodium
Saccharin sodium
Vanillin

6.2 Major 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

Store in the original packaging in order to protect from light.
After opening the blister pocket, replace the remaining portion(s) of tablet in the blister pocket and return the blister to the cardboard carton.
A remaining tablet portion should be given at the next administration.

6.5 Nature and composition of immediate packaging

Box containing aluminium and PVC/aluminium/oPA thermosealed blister of 7 tablets each.

Package sizes:

Box of 1 thermosealed blister of 7 tablets
Box of 2 thermosealed blisters of 7 tablets
Box of 3 thermosealed blisters of 7 tablets
Box of 4 thermosealed blisters of 7 tablets
Box of 5 thermosealed blisters of 7 tablets
Box of 12 thermosealed blisters of 7 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, if appropriate

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

NEXTMUNE ITALY S.R.L.
Via G.B. Benzoni 50
26020 Palazzo Pignano (CR)
Italia

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION

10. DATE OF REVISION OF THE TEXT

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
{carton box}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

K1 KEYVIT 50 mg tablets for dogs (BE, FR, EL, ES, IT, LT, LV, NL, PT, RO)
Vitamin K1 KEYVIT 50 mg tablets or dogs (PL)
Phytomenadione

2. STATEMENT OF ACTIVE SUBSTANCES

Each divisible tablet contains:

Active substance:
Phytomenadione ..... 50.0 mg

3. PHARMACEUTICAL FORM

Tablet.

4. PACKAGE SIZE

7 tablets
14 tablets
21 tablets
28 tablets
35 tablets
84 tablets

5. TARGET SPECIES

Dogs.

6. INDICATION

In dogs: treatment of anticoagulant poisoning, following parenteral treatment.

7. METHOD AND ROUTE OF ADMINISTRATION

Oral use. Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

/

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Store in the original packaging in order to protect from light.
After opening the blister pocket, replace the remaining portion(s) of tablet in the blister pocket and return the blister strip to the cardboard carton.
A remaining tablet portion should be given at the next administration.

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.

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

NEXTMUNE ITALY S.R.L.
Via G.B. Benzoni 50
26020 Palazzo Pignano (CR)
Italia

16. MARKETING AUTHORISATION NUMBER

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
{Blister – PVC/aluminium}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

K1 KEYVIT 50 mg tablets for dogs (BE, FR, EL, ES, IT, LT, LV, NL, PT, RO)
Vitamin K1 KEYVIT 50 mg tablets or dogs (PL)
Phytomenadione

2. NAME OF THE MARKETING AUTHORISATION HOLDER

/

3. EXPIRY DATE

EXP {month/year}

4. BATCH NUMBER

Lot {number}

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

K1 KEYVIT 50 mg tablets for dogs (BE, FR, EL, ES, IT, LT, LV, NL, PT, RO)
Vitamin K1 KEYVIT 50 mg tablets or dogs (PL)

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

Marketing authorisation holder:
NEXTMUNE ITALY S.R.L.
Via G.B. Benzoni 50
26020 Palazzo Pignano (CR)
Italia

Manufacturer responsible for batch release:
Lelypharma B.V.
Zuiveringweg 42
8243 PZ Lelystad
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

K1 KEYVIT 50 mg tablets for dogs (BE, FR, EL, ES, IT, LT, LV, NL, PT, RO)
Vitamin K1 KEYVIT 50 mg tablets or dogs (PL)
Phytomenadione (Vitamin K1)

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

Each tablet contains:

Active substance:
Phytomenadione (Vitamin K1) 50.0 mg

Round, slight yellow quadrisect tablet with 2 crossing scored lines.
The tablet can be divided into halves and quarters.

4. INDICATION(S)

In dogs: treatment of anticoagulant poisoning, following parenteral treatment.

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Very rarely, vomiting and skin disorders, as erythema and dermatitis, or allergic edema have been reported.

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. Alternatively, you can report via your national reporting system {national system details}

7. TARGET SPECIES

Dogs.

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

For oral use.

5 mg phytomenadione per kg bodyweight per day, corresponding to 1 tablet per 10 kg bodyweight per day, once a day, for 21 days, in accordance with the following table:

Bodyweight (kg)	Number of tablets
< 2.5	*¼ tablet*
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*> 7.5 to 10**	*1 tablet*

** Dog > 10 kg: ¼ tablet per 2.5 kg*

Preferably use in non-fasted animals.

Oral treatment should be undertaken within 12 hours after the end of the emergency treatment by the intravenous route (2 intravenous injections of 5 mg phytomenadione (vitamin K1) per kg bodyweight given 12 hours apart). See section "Special warnings for each target species".

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach or children.

Store in the original packaging in order to protect from light.

After opening the blister pocket, replace the remaining portion(s) of tablet in the blister pocket and return the blister strip to the cardboard carton.

A remaining tablet portion should be given at the next administration.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton after [EXP]. The expiry date refers to the last day of that month.

12. SPECIAL WARNING(S)

Special warnings for each target species:

As the anticoagulant effects of rodenticides are known to be long lasting it is recommended to administer vitamin K1 with an oral formulation for 3 weeks. The coagulation status (via one stage prothrombin times) has to be evaluated 48 hours after the last administration. If it is prolonged, the treatment is maintained until the clotting time is normal 48 hours after cessation of treatment to avoid relapse. The duration of treatment can be extended as long as the anticoagulant persists in the body.

Special precautions for use in animals:

The tablets are flavored. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

The formation of prothrombin may be inadequate when dealing with patients with severe liver dysfunction. Therefore, in these animals, careful monitoring of coagulation parameters after administration of the product is required.

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

People with known hypersensitivity to phytomenadione and/or to any other ingredients of the product should avoid contact with the veterinary medicinal product.

Wash hands after use.

Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established in bitches during pregnancy and

lactation. Studies conducted in laboratory animals have shown no teratogenic or foetotoxic effects. Vitamin K1 crosses the placental barrier. Use only according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Salicylates (NSAID) and cephalosporins presenting the N-methyl-thiotetrazole moiety may reduce the effect of vitamin K1, by inhibition of the vitamin K1 recycling.

Overdose (symptoms, emergency procedures, antidotes):
No signs of intolerance were displayed at 3 times the therapeutic dose, administered for 3 weeks.

Incompatibilities:
Not applicable

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Package sizes:
Box of 1 thermosealed blister of 7 tablets
Box of 2 thermosealed blisters of 7 tablets
Box of 3 thermosealed blisters of 7 tablets
Box of 4 thermosealed blisters of 7 tablets
Box of 5 thermosealed blisters of 7 tablets
Box of 12 thermosealed blisters of 7 tablets

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