ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FORTEKOR PLUS 1.25 mg/2.5 mg tablets for dogs
FORTEKOR PLUS 5 mg/10 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:

	pimobendan	benazepril hydrochloride
FORTEKOR PLUS 1.25 mg/2.5 mg tablets	1.25 mg	2.5 mg
FORTEKOR PLUS 5 mg/10 mg tablets	5 mg	10 mg

Excipients:

	iron oxide brown (E172)
FORTEKOR PLUS 1.25 mg/2.5 mg tablets	0.5 mg
FORTEKOR PLUS 5 mg/10 mg tablets	2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.
White and light brown oval bilayer tablets with a score line on both sides.
The tablets can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For the treatment of congestive heart failure due to atrioventricular valve insufficiency or dilated cardiomyopathy in dogs. FORTEKOR PLUS is a fixed dose combination and should only be used in patients whose clinical signs are successfully controlled by administration of the same doses of the individual components (pimobendan and benazepril hydrochloride) given concurrently.

4.3 Contraindications

Do not use in cases of hypertrophic cardiomyopathies or clinical conditions where an augmentation of cardiac output is not possible for functional or anatomical reasons (e.g. aortic or pulmonary stenosis).
Do not use in cases of hypotension, hypovolaemia, hyponatremia or acute renal failure.
Do not use during pregnancy and lactation (see section 4.7).
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

In cases of chronic kidney disease, it is recommended to check the dog's hydration status before starting therapy, and to monitor its plasma creatinine and blood erythrocyte counts during therapy.

As pimobendan is metabolised in the liver, the product should not be administered to dogs with severe hepatic insufficiency.

The efficacy and safety of the product has not been established in dogs below 2.5 kg body weight or under 4 months of age.

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

Wash hands after use.

People with known hypersensitivity to pimobendan or benazepril hydrochloride should avoid contact with the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnant women should take special care to avoid accidental oral exposure because angiotensin converting enzyme (ACE) inhibitors have been found to affect the unborn child during pregnancy in humans.

4.6 Adverse reactions (frequency and seriousness

Pimobendan
A moderate positive chronotropic effect and vomiting may occur in rare cases. However, these effects are dose-dependent and can be avoided by reducing the dose in those cases.

Transient diarrhoea, anorexia or lethargy have been observed in rare cases.

Benazepril hydrochloride
Transient vomiting, incoordination or signs of fatigue have been reported in dogs very rarely, during post authorization experience. In dogs with chronic kidney disease, benazepril may increase plasma creatinine concentrations at the start of therapy very rarely. A moderate increase in plasma creatinine concentrations following administration of ACE inhibitors is compatible with the reduction in glomerular hypertension induced by these agents, and is therefore not necessarily a reason to stop therapy in the absence of other signs.

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

Do not use during pregnancy or lactation.
The safety of the veterinary medicinal product has not been established in breeding, pregnant or lactating dogs.

Laboratory studies in rats and rabbits with pimobendan have shown foetotoxic effects at maternotoxic doses. Laboratory studies in rats and rabbits with pimobendan have not shown any effect on fertility. Laboratory studies in rats have shown that pimobendan is excreted into milk.

Laboratory studies in rats with benazepril have shown foetotoxic effects (foetal urinary tract malformation) at maternally non-toxic doses. It is not known if benazepril is secreted into the milk of lactating bitches.

4.8 Interaction with other medicinal products and other forms of interaction

In dogs with congestive heart failure, benazepril hydrochloride and pimobendan have been given in combination with digoxin and diuretics without demonstrable adverse interactions.

In pharmacological studies no interaction between the cardiac glycoside ouabain and pimobendan was detected. The pimobendan-induced increase in contractility of the heart is attenuated in the presence of the calcium antagonist verapamil and the ß-antagonist propranolol.

In man, the combination of angiotensin converting enzyme (ACE) inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs) can lead to reduced anti-hypertensive efficacy or impaired renal function. Therefore, the concurrent use of FORTEKOR PLUS with NSAIDs or any other medications with a hypotensive effect should be considered carefully before using such combinations.

The combination of FORTEKOR PLUS and other anti-hypertensive agents (e.g. calcium channel blockers, β-blockers or diuretics), anaesthetics or sedatives may lead to additive hypotensive effects. Renal function and signs of hypotension (lethargy, weakness, etc) should be monitored closely and treated as necessary.

Interactions with potassium-sparing diuretics such as spironolactone, triamterene or amiloride cannot be ruled out. It is therefore recommended to monitor plasma potassium levels when using FORTEKOR PLUS in combination with a potassium sparing diuretic because of the risk of hyperkalemia.

4.9 Amounts to be administered and administration route

Oral use.

Dose and treatment schedule:
FORTEKOR PLUS is a fixed combination product which should only be used in dogs which require both active substances to be administered concomitantly at this fixed dose.

The recommended dose range for FORTEKOR PLUS is 0.25–0.5 mg pimobendan per kg body weight and 0.5–1 mg benazepril hydrochloride per kg body weight divided into two daily doses. FORTEKOR PLUS tablets should be administered orally, twice daily 12 hours apart (morning and evening) and approximately 1 hour before feeding.

The tablets are breakable along the score line.

The table below may be used for guidance.

Body weight (kg) of dog	Strength and number of tablets to be administered			
	FORTEKOR PLUS 1.25 mg/2.5 mg tablets		**FORTEKOR PLUS 5 mg/10 mg tablets**	
	Morning	Evening	Morning	Evening
2.5 – 5	0.5	0.5		
5 – 10	1	1		
10 – 20			0.5	0.5
20 – 40			1	1
Over 40 kg			2	2

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

In case of overdose the dog should be treated symptomatically. Transient reversible hypotension may occur in accidental overdose. Therapy should consist of intravenous infusion(s) of warm isotonic saline as required.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: ACE inhibitors, combinations.
ATCvet code: QC09BX90

5.1 Pharmacodynamic properties

Benazepril hydrochloride is a prodrug which is hydrolysed *in vivo* to its active metabolite, benazeprilat. Benazeprilat is a highly potent and selective inhibitor of ACE, thus preventing the conversion of inactive angiotensin I to active angiotensin II and thereby also reducing the synthesis of aldosterone. Therefore, benazepril blocks effects mediated by angiotensin II and aldosterone, including the vasoconstriction of arteries and veins, the retention of sodium and water by the kidney, and remodelling effects (including pathological cardiac hypertrophy and degenerative renal changes).
In dogs with congestive heart failure benazepril hydrochloride reduces the blood pressure and volume load on the heart. Benazepril increased the time to worsening of heart failure, and the time to death, improved clinical condition, reduced cough and improved exercise tolerance in dogs with symptomatic congestive heart failure caused by valvular disease or dilated cardiomyopathy.

Pimobendan, a benzimidazole-pyridazinone derivative, is a non-sympathomimetic, non-glycoside inotropic substance with potent vasodilating properties. It increases the calcium sensitivity of cardiac myofilaments and inhibits phosphodiesterase (type III). It also exhibits a vasodilatory action through the inhibition of phosphodiesterase type III activity.

5.2 Pharmacokinetic particulars

Absorption
Following oral administration of pimobendan alone the absolute bioavailability of the active ingredient is 60–63%. Since this bioavailability is considerably reduced when pimobendan is administered with food or shortly thereafter, it is recommended to treat animals approximately 1 hour before feeding.

After oral administration of benazepril hydrochloride alone, the systemic bioavailability is incomplete (~13%) in dogs due to incomplete absorption (38%) and first pass metabolism. Levels of benazepril decline quickly as the drug is partially metabolised by liver enzymes to benazeprilat. There is no

significant difference in the pharmacokinetics of benazeprilat when benazepril hydrochloride is administered to fed or fasted dogs.
After the oral administration of FORTEKOR PLUS tablets at twice the recommended dose to dogs, peak levels of both compounds are attained rapidly (T_{max} 0.5 h for benazepril hydrochloride and 0.85 h for pimobendan) with peak concentrations (C_{max}) for benazepril hydrochloride of 35.1 ng/ml and 16.5 ng/ml for pimobendan. Peak benazeprilat levels are seen after 1.9 h with peak concentrations (C_{max}) of 43.4 ng/ml.

Distribution
The volume of distribution at steady state is 2.6 l/kg after intravenous administration of pimobendan alone, indicating that pimobendan is distributed readily into the tissues. The mean plasma protein binding *in vitro* is 93%.

Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{1/2}$ = 1.7 h) represents elimination of the free drug, while the terminal phase ($t_{1/2}$ = 19 h) reflects the release of benazeprilat that was bound to ACE, mainly in the tissues. Benazepril and benazeprilat are extensively bound to plasma proteins (85–90%), and in the tissues they are found mainly in the lung, liver and kidney.

Repeated administration of benazepril hydrochloride leads to slight bioaccumulation of benazeprilat (R = 1.47), steady state being achieved within a few days (4 days).

Metabolism
Pimobendan is oxidatively demethylated to its major active metabolite, O-desmethyl pimobendan. Further metabolic pathways are phase II, glucuronides and sulfates.
Benazepril hydrochloride is partially metabolised by liver enzymes to the active metabolite benazeprilat.

Elimination
The plasma elimination half-life of pimobendan when dosed with FORTEKOR PLUS tablets is 0.5 h, consistent with the high clearance of the compound. The main active metabolite of pimobendan is eliminated with a plasma elimination half-life of 2.6 h. Pimobendan is excreted principally in the faeces and to a lesser extent in the urine.

The plasma elimination half-life of benazepril hydrochloride and benazeprilat, when dosed with FORTEKOR PLUS tablets is 0.36 h and 8.36 h, respectively. Benazeprilat is excreted via the biliary (54%) and urinary (46%) routes in dogs. The clearance of benazeprilat is not affected in dogs with impaired renal function; therefore, no adjustment of the FORTEKOR PLUS dose is required in dogs with renal insufficiency.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Artificial Special Dry Flavour
Basic butylated methacrylate copolymer
Copovidone
Croscarmellose sodium
Crospovidone
Dibutyl sebacate
Hypromellose
Iron oxide brown (E172)
Lactose monohydrate
Magnesium stearate
Maize starch
Microcrystalline cellulose

Polysorbate 80
Povidone
Silica, colloidal anhydrous
Silicon dioxide anhydrous
Sodium lauryl sulfate
Starch pregelatinised
Succinic acid
Sucrose

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 24 months.

Any remaining half tablets should be discarded after 1 day.

6.4. Special precautions for storage

Store below 25 °C.
Keep the blister in the outer carton in order to protect from moisture.
Any remaining half tablet should be placed back in the opened blister and stored (for a maximum of 1 day) in the original cardboard carton out of the sight and reach of children.

6.5 Nature and composition of immediate packaging

The tablets are packaged in aluminium/aluminium blisters packaged into an outer cardboard box.

Pack sizes:
FORTEKOR PLUS 1.25 mg/2.5 mg tablets:
Cardboard box containing 30 tablets
Cardboard box containing 60 tablets

FORTEKOR PLUS 5 mg/10 mg tablets:
Cardboard box containing 30 tablets
Cardboard box containing 60 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 materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/15/185/001 (1 x 30 tablets, 1.25 mg/2.5 mg)
EU/2/15/185/002 (1 x 60 tablets, 1.25 mg/2.5 mg)
EU/2/15/185/003 (1 x 30 tablets, 5 mg/10 mg)
EU/2/15/185/004 (1 x 60 tablets, 5 mg/10 mg)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08/09/2015
Date of last renewal: {DD/MM/YYYY}.

10. DATE OF REVISION OF THE TEXT

<{DD month 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

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release
Elanco France S.A.S
26 Rue de la Chapelle
F-68330 Huningue
FRANCE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FORTEKOR PLUS 1.25 mg/2.5 mg tablets for dogs
FORTEKOR PLUS 5 mg/10 mg tablets for dogs

pimobendan/benazepril hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains 1.25 mg pimobendan and 2.5 mg benazepril hydrochloride.
Each tablet contains 5 mg pimobendan and 10 mg benazepril hydrochloride.

3. PHARMACEUTICAL FORM

Tablets

4. PACKAGE SIZE

30 tablets
60 tablets

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) 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 below 25 °C.
Keep the blister in the outer carton in order to protect from moisture.
Any remaining half tablet should be placed back in the opened blister and stored (for a maximum of 1 day) in the original cardboard carton out of the sight and reach of children.

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

Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
Germany

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/15/185/001 (1 x 30 tablets, 1.25 mg/2.5 mg tablets)
EU/2/15/185/002 (1 x 60 tablets, 1.25 mg/2.5 mg tablets)
EU/2/15/185/003 (1 x 30 tablets, 5 mg/10 mg tablets)
EU/2/15/185/004 (1 x 60 tablets, 5 mg/10 mg tablets)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FORTEKOR PLUS 1.25 mg/2.5 mg tablets for dogs
FORTEKOR PLUS 5 mg/10 mg tablets for dogs

pimobendan/benazepril hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco

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:
FORTEKOR PLUS 1.25 mg/2.5 mg tablets for dogs
FORTEKOR PLUS 5 mg/10 mg tablets 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:
Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
Germany

Manufacturer responsible for batch release:
Elanco France S.A.S
26 Rue de la Chapelle
F-68330 Huningue
France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

FORTEKOR PLUS 1.25 mg/2.5 mg tablets for dogs
FORTEKOR PLUS 5 mg/10 mg tablets for dogs

pimobendan/benazepril hydrochloride

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

Each tablet contains

Active substances:

	pimobendan	benazepril hydrochloride
FORTEKOR PLUS 1.25 mg/2.5 mg tablets	1.25 mg	2.5 mg
FORTEKOR PLUS 5 mg/10 mg tablets	5 mg	10 mg

Excipients:

	iron oxide brown E172
FORTEKOR PLUS 1.25 mg/2.5 mg tablets	0.5 mg
FORTEKOR PLUS 5 mg/10 mg tablets	2 mg

The tablets are bilayered, oval, white and light brown, and can be divided into halves along the score line.

4. INDICATION(S)

For the treatment of congestive heart failure due to atrioventricular valve insufficiency or dilated cardiomyopathy in dogs. FORTEKOR PLUS is a fixed dose combination and should only be used in patients whose clinical signs are successfully controlled by administration of the same doses of the individual components (pimobendan and benazepril hydrochloride) given concurrently.

5. CONTRAINDICATIONS

Do not use in cases of cardiac output failure due to aortic or pulmonary stenosis.
Do not use in cases of hypotension (low blood pressure), hypovolemia (low blood volume), hyponatremia (low blood sodium levels) or acute renal (kidney) failure.
Do not use in pregnant or lactating dogs (see section “SPECIAL WARNINGS").
Do not use in cases of hypersensitivity to pimobendan, to benazepril hydrochloride or to any ingredient of the tablets.

6. ADVERSE REACTIONS

Pimobendan:
A moderate positive chronotropic effect and vomiting may occur in rare cases. However, these effects are dose-dependent and can be avoided by reducing the dose in those cases.
Transient diarrhoea, anorexia or lethargy may be observed in rare cases.

Benazepril hydrochloride:
Transient vomiting, incoordination or signs of fatigue have been reported in dogs very rarely, during post authorization experience.
In dogs with chronic kidney disease, benazepril may increase plasma creatinine concentrations at the start of therapy very rarely.
A moderate increase in plasma creatinine concentrations following administration of ACE inhibitors is compatible with the reduction in glomerular hypertension induced by these agents, and is therefore not necessarily a reason to stop therapy in the absence of other signs.

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

Oral use.

FORTEKOR PLUS is a fixed combination product which should only be used in dogs which require both active substances to be administered concomitantly at this fixed dose.

The recommended dose range for FORTEKOR PLUS is 0.25–0.5 mg pimobendan per kg body weight and 0.5–1 mg benazepril hydrochloride per kg body weight divided into two daily doses. FORTEKOR PLUS tablets should be administered orally, twice daily 12 hours apart (morning and evening) and approximately 1 hour before feeding.

The tablets are breakable along the score line.

The table below may be used for guidance.

Body weight (kg) of dog	Strength and number of tablets to be administered			
	FORTEKOR PLUS 1.25 mg/2.5 mg tablets		**FORTEKOR PLUS 5 mg/10 mg tablets**	
	Morning	Evening	Morning	Evening
2.5 – 5	0.5	0.5		
5 – 10	1	1		
10 – 20			0.5	0.5
20 – 40			1	1
Over 40 kg			2	2

9. ADVICE ON CORRECT ADMINISTRATION

FORTEKOR PLUS tablets can be divided into halves if needed.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store below 25 °C.
Keep the blister in the outer carton in order to protect from moisture.

Any remaining half tablet should be placed back in the opened blister and stored (for a maximum of 1 day) in the original cardboard carton out of the sight and reach of children.

Do not use this veterinary medicinal product after the expiry date which is stated on the blister and carton after EXP.

12. SPECIAL WARNING(S)

Special precautions for use in animals
In cases of chronic kidney disease, it is recommended to check the hydration status before starting therapy, and to monitor plasma creatinine and blood erythrocyte counts during therapy.

As pimobendan is metabolised in the liver, the product should not be administered in dogs with severe hepatic insufficiency.

The efficacy and safety of the product has not been established in dogs below 2.5 kg body weight or under 4 months of age.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use.

People with known hypersensitivity to pimobendan or benazepril hydrochloride should avoid contact with the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnant women should take special care to avoid accidental oral exposure because angiotensin converting enzyme (ACE) inhibitors have been found to affect the unborn child during pregnancy in humans.

Pregnancy and lactation:
Do not use during pregnancy or lactation. The safety of the veterinary medicinal product has not been established in breeding, pregnant or lactating dogs.

Interactions with other medicinal products and other forms of interaction:
Inform the veterinary surgeon if the animal is taking, or has recently taken, any other medicines.

In dogs with congestive heart failure, benazepril hydrochloride and pimobendan have been given in combination with digoxin and diuretics without demonstrable adverse interactions.

In humans, the combination of ACE inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs) can lead to reduced anti-hypertensive efficacy or impaired kidney function. Therefore the concurrent use of FORTEKOR PLUS with NSAIDs or any other medications with a hypotensive effect should be considered carefully before using such combinations.

The combination of FORTEKOR PLUS and other anti-hypertensive agents (e.g. calcium channel blockers, β-blockers or diuretics), anaesthetics or sedatives may lead to additive hypotensive effects. Your veterinary surgeon may recommend to closely monitor kidney function and for signs of hypotension (lethargy, weakness etc) and treat these if necessary.

Interactions with potassium-preserving diuretics like spironolactone, triamterene or amiloride cannot be ruled out. Your veterinary surgeon may therefore recommend the monitoring of plasma potassium concentrations when using FORTEKOR PLUS in combination with a potassium-sparing diuretic because of the risk of hyperkalaemia (high blood potassium).

Overdose (symptoms, emergency procedures, antidotes):
In case of overdose the dog should be treated symptomatically. Transient reversible hypotension (low blood pressure) may occur in accidental overdose. Therapy should consist of intravenous infusion(s) of warm isotonic saline as required.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon or your 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

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

15. OTHER INFORMATION

Pack Sizes:

FORTEKOR PLUS 1.25 mg/2.5 mg tablets:
Cardboard box containing 30 tablets
Cardboard box containing 60 tablets

FORTEKOR PLUS 5 mg/10 mg tablets:
Cardboard box containing 30 tablets
Cardboard box containing 60 tablets

Not all pack sizes may be marketed.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

ANNEX IV

GROUNDS FOR REFUSAL OF ONE OF THE VARIATIONS IN THE GROUP OF APPLICATIONS SUBMITTED BY THE MAH

Conclusions presented by the European Medicines Agency:

The CVMP has recommended the refusal of the below variation to the terms of the marketing authorisation for Fortekor Plus.

Variation(s) refused		**Annex(es) affected**
F.II.d.1.a	Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	N/A

F.II.d.1.a: Change outside the approved specifications limits range - increase the total related substances acceptance criterion from “not more than 5.0%” to “not more than 7.5%”: *The proposed limit is not supported by the real-time stability data.*