[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketexx 100 mg/ml solution for injection (BG, CY, CZ, EE, EL, ES, FR, HR, HU, IE, IT, LT, LV, NL, PL, PT, RO, SI, SK, UK(NI))
Ketexx Vet 100 mg/ml solution for injection (BE, DK, FI, IS, LU, NO, SE)
Ketexx 100 mg/ml solution for injection for dogs, cats, cattle, sheep, goats, horses, guinea pigs, hamsters, rabbits, rats and mice (AT, DE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Ketamine 100.0 mg
(equivalent to 115.3 mg ketamine hydrochloride)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzethonium chloride	0.11 mg
Water for injections	

.
Clear, colourless aqueous and, practically free from visible particles solution for injection.

3. CLINICAL INFORMATION

3.1 Target species

Dogs, cats, cattle, sheep, goats, horses, guinea pigs, hamsters, rabbits (exclusively kept as pets), rats, mice.

3.2 Indications for use for each target species

The veterinary medicinal product may be used in combination with a sedative for:
- Immobilisation
- Sedation
- General anaesthesia

3.3 Contraindications

Do not use in cases of severe hypertension, cardio-respiratory deficiency, or hepatic or renal dysfunction.
Do not use in animals with glaucoma.
Do not use in animals with eclampsia or pre-eclampsia.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use as a sole anaesthetic agent in any of the target species.
Do not use in ocular surgical interventions.
Do not use for surgical intervention on pharynx, larynx, trachea or bronchial tree, if sufficient relaxation is not ensured by administration of a muscle relaxant (intubation obligatory).
Do not use in animals undergoing a myelogram procedure.
Do not use in cases of pheochromocytoma or untreated hyperthyroidism.

Do not use in cases of head trauma and increased intracerebral pressure.

3.4 Special warnings

For very painful and major surgical interventions, as well as for maintenance of anaesthesia, a combination with injectable or inhalational anaesthetics is indicated.
As muscle relaxation required for surgical procedures cannot be achieved with ketamine alone, additional muscle-relaxants should be used concomitantly.
For improvement of anaesthesia or prolongation of effect, ketamine can be combined with α2-receptor-agonists, anaesthetics, neuroleptanalgesics, tranquillisers and inhalational anaesthetic agents.

3.5 Special precautions for use

Special precautions for safe use in the target species:
A small proportion of animals have been reported to be unresponsive to ketamine as an anaesthetic agent at normal dosages.
Use of premedicants should be followed by a suitable reduction in dosage.
In the cat and dog, the eyes remain open and the pupils dilated. The eyes may be protected by covering with a damp gauze swab or using appropriate ointments.
Ketamine may exhibit pro-convulsant and anti-convulsant properties, and therefore should be used with care in patients with seizure disorders.
Ketamine may increase intracranial pressure and therefore, may not be suitable for patients with cerebrovascular insults.
When used in combination with other veterinary medicinal products, consult the contraindications and warnings that appear on the relevant data sheets.
The eyelid reflex stays intact.
Twitching, as well as excitation upon recovery, may be possible. It is important that both premedication and recovery should occur in quiet and calm surroundings. To ensure a smooth recovery appropriate analgesia and premedication should be administered, if indicated.
The concomitant use of other pre-anaesthetics or anaesthetics should be subject to a benefit-risk assessment, taking into account the composition of the used medicines and their doses and the nature of the intervention. The recommended doses of ketamine are likely to vary depending on the concomitant pre-anaesthetics and anaesthetics used.
The prior administration of an anticholinergic such as atropine or glycopyrrolate to prevent the occurrence of adverse effects, especially hypersalivation, may be considered after a benefit-risk assessment by the veterinarian.
Ketamine should be used with caution when pulmonary disease is present or suspected.
Animals should be fasted for a period prior to anaesthesia where possible.
In small rodents cooling down should be prevented.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This is a potent drug. Particular care should be taken to avoid accidental self-injection.
In case of accidental self-injection or if symptoms develop after ocular/oral contact, seek medical advice immediately and show the package leaflet or the label to the physician, but DO NOT DRIVE, as sedation may occur.
Avoid contact with the skin and eyes. Wash any splashes from skin and eyes immediately with large amounts of water.
Adverse effects on the foetus cannot be excluded. Pregnant women should avoid handling the veterinary medicinal product.
People with known hypersensitivity to ketamine or any of the excipients should avoid contact with the veterinary medicinal product.

Advice to physician:
Do not leave patient unattended. Maintain airways and give symptomatic and supportive treatment.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension[1]; Dyspnoea[1], bradypnoea[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Increased heart rate, high blood pressure[2]; Respiratory depression[3]; Ataxia[4], hyperaesthesia [4], hypertonia, mydriasis[5], nystagmus[5], excitation[4].

[1] mainly during and after the recovery phase.
[2] with concurrent increased bleeding tendency.
[3] dose-dependent; can lead to respiratory arrest. The combination of respiratory depressants can amplify this effect.
[4] on awakening.
[5] the eyes remain open.

Cats:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension[1]; Dyspnoea[1], bradypnoea[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Increased heart rate; Respiratory depression[2]; Hypertonia, mydriasis[3], nystagmus[3]; Immediate pain upon injection[4].

[1] mainly during and after the recovery phase.
[2] dose-dependent; can lead to respiratory arrest. The combination of respiratory depressants can amplify this effect.
[3] the eyes remain open.
[4] during intra-muscular injections.

Horses:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension[1]; Dyspnoea[1], bradypnoea[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1], ataxia[2], hyperaesthesia [2], excitation[2], pupil disorder[1]; Hypersalivation[1.]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypertonia.

[1] mainly during and after the recovery phase.
[2] on awakening.

Pet rabbits, cattle, goats:

Rare	Cardiac arrest[1], hypotension[1]; Dyspnoea[1], bradypnoea[1], pulmonary oedema[1];

(1 to 10 animals / 10,000 animals treated):	Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Respiratory depression[2]; Hypertonia.

[1] mainly during and after the recovery phase.
[2] dose-dependent; can lead to respiratory arrest. The combination of respiratory depressants can amplify this effect.

Sheep, guinea pigs, hamsters, rats, mice:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension[1]; Dyspnoea[1], bradypnoea[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].

[1] mainly during and after the recovery phase.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Pregnancy and lactation:
Ketamine passes the blood placenta barrier very well to enter the foetal blood circulation in which 75 to 100% of the maternal blood levels can be reached. This partially anaesthetises neonates delivered by caesarean section.
Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Neuroleptics, tranquillisers, cimetidine and chloramphenicol increase the anaesthetic effect of ketamine (also see section 3.4 special warnings).
Barbiturates, opiates and diazepam may prolong time to recovery.
Effects may be cumulative. A decrease of the dose of one or both agents may be necessary.
There is a possibility of an increased risk of cardiac arrhythmia when ketamine is used in combination with thiopental or halothane. Halothane prolongs the half-life of ketamine.
Simultaneous intravenous administration of a spasmolytic agent may provoke a collapse.
Theophylline, when given with ketamine, may provoke an increase of epileptic crises.
When detomidine is used together with ketamine, the recovery is slower than when ketamine is used alone.

3.9 Administration routes and dosage

Dogs, cats, cattle, horses: slow intravenous and intramuscular use;
Guinea pigs, hamsters, pet rabbits, rats and mice: intraperitoneal use, slow intravenous and intramuscular use.
Sheep and goats: slow intravenous use.

Ketamine should be combined with a sedative.

One dose of 10 mg of ketamine per kg bodyweight corresponds to 0.1 ml of the veterinary medicinal product per kg bodyweight.
To ensure a correct dosage, body weight should be determined as accurately as possible.
Before ketamine is administered, please ensure that the animals are adequately sedated.

For intramuscular injection in cattle and horses a maximum volume per injection site is 20 ml.
Ketamine can show large inter-individual variation in effect, and therefore dose rates administered should be tailored to the individual animal, dependent on factors such as age, condition, and the depth and duration of anaesthesia required.

The following dosing advices provide possible combinations with ketamine, the concomitant use of other pre-anaesthetics, anaesthetics or sedatives should be subject to a benefit-risk assessment by the responsible veterinarian.

Dogs
Combination with xylazine or medetomidine:
Intramuscular use:
Xylazine (1.1 mg/kg i.m.) or medetomidine (10 to 30 µg/kg i.m.) can be used with ketamine (5 to 10 mg/kg i.e. 0.5 to 1 ml/10 kg i.m.) for short term anaesthesia of 25 to 40 minutes. The ketamine dose can be adjusted, depending on the desired duration of surgery.
Intravenous use:
In case of intravenous use, the dose must be reduced to 30 – 50% of the recommended intramuscular dose.

Cats
Combination with xylazine:
Xylazine (0.5 to 1.1 mg/kg i.m.) with or without atropine is administered 20 minutes before ketamine (11 to 22 mg/kg i.m. i.e. 0.11 to 0.22 ml/kg i.m.).

Combination with medetomidine:
Medetomidine (10 to 80 µg/kg i.m.) can be combined with ketamine (2.5 to 7.5 mg/kg i.m. i.e. 0.025 to 0.075 ml/kg i.m.). The dose of ketamine should be reduced as the dose of medetomidine increases.

Horses
Combination with detomidine:
Detomidine 20 µg/kg i.v., after 5 minutes ketamine 2.2 mg/kg fast i.v. (2.2 ml/100 kg i.v.).
Onset of action is gradual, taking approximately 1 minute to attain recumbency, with duration of anaesthetic effect lasting approximately 10 – 15 minutes.

Combination with xylazine:
Xylazine 1.1 mg/kg i.v., followed by ketamine 2.2 mg/kg i.v. (2.2 ml/100 kg i.v.).
Onset of action is gradual, taking approximately 1 minute, with duration of anaesthetic effect being variable and lasting 10 – 30 minutes but usually less than 20 minutes.
After injection the horse lays down spontaneously without any further help. If a distinct muscle relaxation is required simultaneously, muscle relaxants can be administered to the recumbent animal, until the horse shows first symptoms of relaxation.

Cattle
Combination with xylazine:
Intravenous use:
Adult cattle can be anaesthetised for short periods with xylazine (0.1 mg/kg i.v.) followed by ketamine (2 mg/kg i.v. i.e. 2 ml/100 kg i.v.). Anaesthesia lasts approximately 30 minutes but can be prolonged for 15 minutes with additional ketamine (0.75 to 1.25 mg/kg i.v. i.e. 0.75 to 1.25 ml/100 kg i.v.).
Intramuscular use:
Ketamine and xylazine doses should be doubled in case of intramuscular use.

Sheep and goats

Intravenous use:
Ketamine 0.5 to 7 mg/kg i.v. i.e. 0.05 to 0.7 ml/10 kg i.v. depending on the sedative used.

Pet rabbits and rodents
Combination with xylazine:
Pet rabbits: xylazine (5-10 mg/kg i.m.) + ketamine (35-50 mg/kg i.m. i.e. 0.35 to 0.50 ml/kg i.m.).
Rats: xylazine (5-10 mg/kg i.p., i.m.) + ketamine (40-80 mg/kg i.p., i.m. i.e. 0.4 to 0.8 ml/kg i.p., i.m.).
Mice: xylazine (7.5-16 mg/kg i.p.) + ketamine (90-100 mg/kg i.p. i.e. 0.9 to 1.0 ml/kg i.p.).
Guinea pigs: xylazine (0.1-5 mg/kg i.m.) + ketamine (30-80 mg/kg i.m. i.e. 0.3 to 0.8 ml/kg i.m.).
Hamsters: xylazine (5-10 mg/kg i.p.) + ketamine (50-200 mg/kg i.p. i.e. 0.5 to 2 ml/kg i.p.).

Dose for maintenance of anaesthesia: when needed, prolongation of effect is possible by repeated administration of an optionally reduced initial dose.

The stopper can be broached up to 30 times. The user should choose the most appropriate vial size according to the target species to be treated and the administration route.

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

In case of overdose CNS effects (e.g. seizures), apnoea, cardiac arrhythmia, dysphagia and respiratory depression or paralysis may occur.
If necessary, suitable artificial aids to maintain ventilation and cardiac output should be used until sufficient detoxification has taken place. Pharmacological cardiac stimulants are not recommended, unless no other supportive measures are available.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

3.12 Withdrawal periods

Cattle, sheep, goats and horses:
Meat and offal: 1 day.
Milk: zero hours.

Not authorised for use in rabbits for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN01AX03

4.2 Pharmacodynamics

Ketamine blocks nerve impulses in the cerebral cortex while activating subjacent brain regions. Hence, a dissociative anaesthesia is obtained, on the one hand narcosis and superficial analgesia and, on the other hand no bulbar depression, continued muscle tone and maintenance of certain reflexes (e.g. swallowing reflex).
At anaesthetic doses, ketamine is a bronchodilator (sympathomimetic effect), increases heart rate and blood pressure, and increases cerebral circulation and intraocular pressure.
These characteristics can be modified if the veterinary medicinal product is used in association with other anaesthetics.

4.3 Pharmacokinetics

Ketamine is rapidly distributed in the organism. The plasma protein binding of ketamine is 50%. Ketamine shows affinity to certain tissues, and increased concentrations have been found in the liver and kidneys. The majority of ketamine is excreted via kidney. Ketamine is extensively metabolised, however species specific characteristics can be observed.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale (10 ml vials): 5 years.
Shelf life of the veterinary medicinal product as packaged for sale (20 ml and 50 ml vials): 4 years.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Brown type I glass vials containing 10 ml, 20 ml and 50 ml veterinary medicinal product, closed with a bromobutyl rubber stopper and aluminium cap.

Pack sizes:
Carton box holding 1 vial of 10 ml, 20 ml or 50 ml
Carton box holding 5 vials of 10 ml, 20 ml or 50 ml
Polystyrene box holding 35 vials of 10 ml
Polystyrene box holding 28 vials of 20 ml
Polystyrene box holding 15 vials of 50 ml

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

{DD/MM/YYYY}

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

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

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

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton box / polystyrene box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketexx 100 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Ketamine 100.0 mg/ml(equivalent to 115.3 mg/ml ketamine hydrochloride)

3. PACKAGE SIZE

10 ml
20 ml
50 ml
5 x 10 ml
5 x 20 ml
5 x 50 ml
35 x 10 ml
28 x 20 ml
15 x 50 ml

4. TARGET SPECIES

Dogs, cats, cattle, sheep, goats, horses, guinea pigs, hamsters, rabbits (exclusively kept as pets), rats, mice.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

For i.v., i.m. and i.p. use.

7. WITHDRAWAL PERIODS

Withdrawal period:
Cattle, sheep, goats and horses:
Meat and offal: 1 day.
Milk: zero hours.

Not authorised for use in rabbits for human consumption.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use by: 28 days.

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Glass vials of 10 ml, 20 ml or 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketexx

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Ketamine 100.0 mg/ml(equivalent to 115.3 mg/ml ketamine hydrochloride)

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within 28 days.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Ketexx 100 mg/ml solution for injection (BG, CY, CZ, EE, EL, ES, FR, HR, HU, IE, IT, LT, LV, NL, PL, PT, RO, SI, SK, UK(NI))
Ketexx Vet 100 mg/ml solution for injection (BE, DK, FI, IS, LU, NO, SE)
Ketexx 100 mg/ml solution for injection for dogs, cats, cattle, sheep, goats, horses, guinea pigs, hamsters, rabbits, rats and mice (AT, DE)

2. Composition

Each ml contains:

Active substance:
Ketamine 100.0 mg
(equivalent to 115.3 mg ketamine hydrochloride)

Excipient(s):
Benzethonium chloride 0.11 mg

Clear, colourless aqueous and, practically free from visible particles solution for injection.

3. Target species

Dogs, cats, cattle, sheep, goats, horses, guinea pigs, hamsters, rabbits (exclusively kept as pets), rats, mice.

4. Indications for use

The veterinary medicinal product may be used in combination with a sedative for:
- Immobilisation
- Sedation
- General anaesthesia

5. Contraindications

Do not use in cases of severe hypertension, cardio-respiratory deficiency, or hepatic or renal dysfunction.
Do not use in animals with glaucoma.
Do not use in animals with eclampsia or pre-eclampsia.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use as a sole anaesthetic agent in any of the target species.
Do not use in ocular surgical interventions.
Do not use for surgical intervention on pharynx, larynx, trachea or bronchial tree, if sufficient relaxation is not ensured by administration of a muscle relaxant (intubation obligatory).
Do not use in animals undergoing a myelogram procedure.
Do not use in cases of pheochromocytoma or untreated hyperthyroidism.
Do not use in cases of head trauma and increased intracerebral pressure.

6. Special warnings

Special warnings:
For very painful and major surgical interventions, as well as for maintenance of anaesthesia, a combination with injectable or inhalational anaesthetics is indicated.
As muscle relaxation required for surgical procedures cannot be achieved with ketamine alone, additional muscle-relaxants should be used concomitantly.
For improvement of anaesthesia or prolongation of effect, ketamine can be combined with α2-receptor-agonists, anaesthetics, neuroleptanalgesics, tranquillisers and inhalational anaesthetic agents.

Special precautions for safe use in the target species:
A small proportion of animals have been reported to be unresponsive to ketamine as an anaesthetic agent at normal dosages. Use of premedicants should be followed by a suitable reduction in dosage.
In the cat and dog, the eyes remain open and the pupils dilated. The eyes may be protected by covering with a damp gauze swab or using appropriate ointments.
Ketamine may exhibit pro-convulsant and anti-convulsant properties, and therefore should be used with care in patients with seizure disorders.
Ketamine may increase intracranial pressure and therefore, may not be suitable for patients with cerebrovascular insults.
When used in combination with other veterinary medicinal products, consult the contraindications and warnings that appear on the relevant data sheets.
The eyelid reflex stays intact.
Twitching, as well as excitation upon recovery, may be possible. It is important that both premedication and recovery should occur in quiet and calm surroundings. To ensure a smooth recovery appropriate analgesia and premedication should be administered, if indicated.
The concomitant use of other pre-anaesthetics or anaesthetics should be subject to a benefit-risk assessment, taking into account the composition of the used medicines and their doses and the nature of the intervention. The recommended doses of ketamine are likely to vary depending on the concomitant pre-anaesthetics and anaesthetics used.
The prior administration of an anticholinergic such as atropine or glycopyrrolate to prevent the occurrence of adverse effects, especially hypersalivation, may be considered after a benefit-risk assessment by the veterinarian.
Ketamine should be used with caution when pulmonary disease is present or suspected.
Animals should be fasted for a period prior to anaesthesia where possible.
In small rodents cooling down should be prevented.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This is a potent drug. Particular care should be taken to avoid accidental self-injection.
In case of accidental self-injection or if symptoms develop after ocular/oral contact, seek medical advice immediately and show the package leaflet or the label to the physician, but DO NOT DRIVE, as sedation may occur.
Avoid contact with the skin and eyes. Wash any splashes from skin and eyes immediately with large amounts of water.
Adverse effects on the foetus cannot be excluded. Pregnant women should avoid handling the veterinary medicinal product.
People with known hypersensitivity to ketamine or any of the excipients should avoid contact with the veterinary medicinal product.

Advice to physician:
Do not leave patient unattended. Maintain airways and give symptomatic and supportive treatment.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
Ketamine passes the blood placenta barrier very well to enter the foetal blood circulation in which 75 to 100% of the maternal blood levels can be reached. This partially anaesthetises neonates delivered by caesarean section.

Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Neuroleptics, tranquillisers, cimetidine and chloramphenicol increase the anaesthetic effect of ketamine (also see the section on special warnings).
Barbiturates, opiates and diazepam may prolong time to recovery.
Effects may be cumulative. A decrease of the dose of one or both agents may be necessary.
There is a possibility of an increased risk of cardiac arrhythmia when ketamine is used in combination with thiopental or halothane. Halothane prolongs the half-life of ketamine.
Simultaneous intravenous administration of a spasmolytic agent may provoke a collapse.
Theophylline, when given with ketamine, may provoke an increase of epileptic crises.
When detomidine is used together with ketamine, the recovery is slower than when ketamine is used alone.

Overdose:
In case of overdose CNS effects (e.g. seizures), apnoea, cardiac arrhythmia, dysphagia and respiratory depression or paralysis may occur.
If necessary, suitable artificial aids to maintain ventilation and cardiac output should be used until sufficient detoxification has taken place. Pharmacological cardiac stimulants are not recommended, unless no other supportive measures are available.

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product should not be mixed with other veterinary medicinal products.

7. Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension (low blood pressure)[1]; Dyspnoea (difficulty breathing)[1], bradypnoea (slow breathing rate)[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Increased heart rate, high blood pressure[2]; Respiratory depression[3]; Ataxia (incoordination)[4], hyperaesthesia (increased sensitivity to stimuli)[4], hypertonia, mydriasis (dilated pupils)[5], nystagmus[5], excitation[4].

[1] mainly during and after the recovery phase.
[2] with concurrent increased bleeding tendency.
[3] dose-dependent; can lead to respiratory arrest. The combination of respiratory depressants can amplify this effect.
[4] on awakening.
[5] the eyes remain open.

Cats:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension (low blood pressure)[1]; Dyspnoea (difficulty breathing)[1], bradypnoea (slow breathing rate)[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].
Very rare	Increased heart rate;

(<1 animal / 10,000 animals treated, including isolated reports):	Respiratory depression[2]; Hypertonia, mydriasis (dilated pupils)[3], nystagmus[3]; Immediate pain upon injection[4].

[1] mainly during and after the recovery phase.
[2] dose-dependent; can lead to respiratory arrest. The combination of respiratory depressants can amplify this effect.
[3] the eyes remain open.
[4] during intra-muscular injections.

Horses:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension (low blood pressure)[1]; Dyspnoea (difficulty breathing)[1], bradypnoea (slow breathing rate)[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1], ataxia (incoordination)[2], hyperaesthesia (increased sensitivity to stimuli)[2], excitation[2], pupil disorder[1]; Hypersalivation[1.]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypertonia.

[1] mainly during and after the recovery phase.
[2] on awakening.

Pet rabbits, cattle, goats:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension (low blood pressure)[1]; Dyspnoea (difficulty breathing)[1], bradypnoea (slow breathing rate)[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Respiratory depression[2]; Hypertonia.

[1] mainly during and after the recovery phase.
[2] Dose-dependent; can lead to respiratory arrest. The combination of respiratory depressants can amplify this effect.

Sheep, guinea pigs, hamsters, rats, mice:

Rare (1 to 10 animals / 10,000 animals treated):	Cardiac arrest[1], hypotension (low blood pressure)[1]; Dyspnoea (difficulty breathing)[1], bradypnoea (low breathing rate)[1], pulmonary oedema[1]; Prostration[1], convulsion[1], tremor[1]; Hypersalivation[1]; Pupil disorder[1].

[1] mainly during and after the recovery phase.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: national system details.

8. Dosage for each species, routes and method of administration

Dogs, cats, cattle, horses:	slow intravenous (i.v.) and intramuscular (i.m.) use;
Guinea pigs, hamsters, pet rabbits, rats and mice:	intraperitoneal (i.p.) use, slow intravenous and intramuscular use.
Sheep and goats:	slow intravenous use.

Ketamine should be combined with a sedative.
One dose of 10 mg of ketamine per kg bodyweight corresponds to 0.1 ml of the veterinary medicinal product per kg bodyweight.
To ensure a correct dosage, body weight should be determined as accurately as possible.
Before ketamine is administered, please ensure that the animals are adequately sedated.

The following dosing advices provide possible combinations with ketamine, the concomitant use of other pre-anaesthetics, anaesthetics or sedatives should be subject to a benefit-risk assessment by the responsible veterinarian.

Dogs
Combination with xylazine or medetomidine:
Intramuscular use:
Xylazine (1.1 mg/kg i.m.) or medetomidine (10 to 30 µg/kg i.m.) can be used with ketamine (5 to 10 mg/kg i.e. 0.5 to 1 ml/10 kg i.m.) for short term anaesthesia of 25 to 40 minutes. The ketamine dose can be adjusted, depending on the desired duration of surgery.
Intravenous use:
In case of intravenous use, the dose must be reduced to 30 – 50% of the recommended intramuscular dose.

Cats
Combination with xylazine:
Xylazine (0.5 to 1.1 mg/kg i.m.) with or without atropine is administered 20 minutes before ketamine (11 to 22 mg/kg IM i.e. 0.11 to 0.22 ml/kg i.m.).

Combination with medetomidine:
Medetomidine (10 to 80 µg/kg i.m.) can be combined with ketamine (2.5 to 7.5 mg/kg i.m. i.e. 0.025 to 0.075 ml/kg i.m.). The dose of ketamine should be reduced as the dose of medetomidine increases.

Horses
Combination with detomidine:
Detomidine 20 µg/kg i.v., after 5 minutes ketamine 2.2 mg/kg fast i.v. (2.2 ml/100 kg i.v.).
Onset of action is gradual, taking approximately 1 minute to attain recumbency, with duration of anaesthetic effect lasting approximately 10 – 15 minutes.

Combination with xylazine:
Xylazine 1.1 mg/kg i.v., followed by ketamine 2.2 mg/kg i.v. (2.2 ml/100 kg i.v.).
Onset of action is gradual, taking approximately 1 minute, with duration of anaesthetic effect being variable and lasting 10 – 30 minutes but usually less than 20 minutes.
After injection the horse lays down spontaneously without any further help. If a distinct muscle relaxation is required simultaneously, muscle relaxants can be administered to the recumbent animal, until the horse shows first symptoms of relaxation.

Cattle
Combination with xylazine:
Intravenous use:
Adult cattle can be anaesthetised for short periods with xylazine (0.1 mg/kg i.v.) followed by ketamine (2 mg/kg IV i.e. 2 ml/100 kg i.v.). Anaesthesia lasts approximately 30 minutes but can be prolonged for 15 minutes with additional ketamine (0.75 to 1.25 mg/kg i.v. i.e. 0.75 to 1.25 ml/100 kg i.v.).

Intramuscular use:
Ketamine and xylazine doses should be doubled in case of intramuscular use.

Sheep and goats
Intravenous use:
Ketamine 0.5 to 7 mg/kg i.v. i.e. 0.05 to 0.7 ml/10 kg i.v. depending on the sedative used.

Pet rabbits and rodents
Combination with xylazine:
Pet rabbits: xylazine (5-10 mg/kg i.m.) + ketamine (35-50 mg/kg i.m.i.e. 0.35 to 0.50 ml/kg i.m.).
Rats: xylazine (5-10 mg/kg i.p., i.m.) + ketamine (40-80 mg/kg i.p., i.m. i.e. 0.4 to 0.8 ml/kg i,p., i.m.).
Mice: xylazine (7.5-16 mg/kg i.p.) + ketamine (90-100 mg/kg i.p. i.e. 0.9 to 1.0 ml/kg i.p.).
Guinea pigs: xylazine (0.1-5 mg/kg i.m.) + ketamine (30-80 mg/kg i.m. i.e. 0.3 to 0.8 ml/kg i.m.).
Hamsters: xylazine (5-10 mg/kg i.p.) + ketamine (50-200 mg/kg i.p. i.e. 0.5 to 2 ml/kg i.p.).

Dose for maintenance of anaesthesia: when needed, prolongation of effect is possible by repeated administration of an optionally reduced initial dose.

9. Advice on correct administration

For intramuscular injection in cattle and horses a maximum volume per injection site is 20 ml.

Ketamine can show large inter-individual variation in effect, and therefore dose rates administered should be tailored to the individual animal, dependent on factors such as age, condition, and the depth and duration of anaesthesia required.

The stopper can be broached up to 30 times. The user should choose the most appropriate vial size according to the target species to be treated and the administration route.

10. Withdrawal periods

Cattle, sheep, goats and horses:
Meat and offal: 1 day.
Milk: zero hours.

Not authorised for use in rabbits for human consumption.

11. Special storage precautions

Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and the carton after Exp.. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Brown type I glass vials containing 10 ml, 20 ml and 50 ml veterinary medicinal product, closed with a bromobutyl rubber stopper and aluminium cap.

Pack sizes:
Carton box holding 1 vial of 10 ml, 20 ml or 50 ml
Carton box holding 5 vials of 10 ml, 20 ml or 50 ml
Polystyrene box holding 35 vials of 10 ml
Polystyrene box holding 28 vials of 20 ml
Polystyrene box holding 15 vials of 50 ml

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:
Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands
Tel: +31(0)348 416945

Local representatives and contact details to report suspected adverse reactions:

17. Other information