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 (DK, FI, IS, 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)
Ketasan 100 mg/ml solution for injection (BE, LU)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

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

Excipient(s):
Benzethonium chloride 0.11 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

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

4. CLINICAL PARTICULARS

4.1 Target species

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

4.2 Indications for use, specifying the target species

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

4.3 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 known 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.

4.4 Special warnings for each target species

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.

4.5 Special precautions for use

Special precautions for use in animals
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 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.
People with known hypersensitivity to ketamine or any of the excipients should avoid contact with the veterinary medicinal product.
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.
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.

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

4.6 Adverse reactions (frequency and seriousness)

In anaesthetised animals, mainly during and after the recovery phase, cardio-respiratory disorders (cardiac arrest, hypotension, dyspnoea, bradypnea, pulmonary oedema) associated or not with neurological disorders (convulsions, prostration, tremors) and systemic disorders (hypersalivation, pupillary abnormality) have been observed in rare cases.
Reactions on awakening – ataxia, hypersensitivity to stimuli, excitement – have been rarely and very rarely reported in horses and dogs, respectively.
Salivation has been very rarely reported in cats.
An increase in skeletal muscle tone has been very rarely reported in cats, dogs, horses, rabbits, cattle and goats.
Dose-dependent respiratory depression, which can lead to respiratory arrest, has been very rarely reported in cats, dogs, rabbits, cattle and goats. The combination of respiratory depressants can amplify this effect.
An increase in heart rate has been reported very rarely in cats and dogs. Increased arterial blood pressure with concurrent increased bleeding tendency in dogs has been very rarely reported.
In dogs and cats, in very rare cases, the eyes remain open, with mydriasis and nystagmus.
Pain during intramuscular injection has been very rarely reported in cats.
All adverse reactions and their frequencies come from pharmacovigilance declarations.

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

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. The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Neuroleptics, tranquillisers, cimetidine and chloramphenicol increase the anaesthetic effect of ketamine (also see section 4.4).
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.

4.9 Amounts to be administered and administration route

Dogs, cats, cattle, horses, guinea pigs, hamsters, rabbits, rats and mice: for slow intravenous and intramuscular administration. In guinea pigs, hamsters, rabbits, rats and mice, the intraperitoneal route can also be used.
Sheep and goats: for slow intravenous administration.

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.

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.
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 IM) or medetomidine (10 to 30 µg/kg IM) can be used with ketamine (5 to 10 mg/kg i.e. 0.5 to 1 ml/10 kg IM) 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 IM) 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 IM).

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

Horses
Combination with detomidine:
Detomidine 20 µg/kg IV, after 5 minutes ketamine 2.2 mg/kg fast IV (2.2 ml/100 kg IV).
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 IV, followed by ketamine 2.2 mg/kg IV (2.2 ml/100 kg IV).
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 IV) followed by ketamine (2 mg/kg IV i.e. 2 ml/100 kg IV). Anaesthesia lasts approximately 30 minutes but can be prolonged for 15 minutes with additional ketamine (0.75 to 1.25 mg/kg IV i.e. 0.75 to 1.25 ml/100 kg IV).
Intramuscular use:
Ketamine and xylazine doses should be doubled in case of intramuscular administration.

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

Rabbits and rodents
Combination with xylazine:

Rabbits: xylazine (5-10 mg/kg IM) + ketamine (35-50 mg/kg IM i.e. 0.35 to 0.50 ml/kg IM).
Rats: xylazine (5-10 mg/kg IP, IM) + ketamine (40-80 mg/kg IP, IM i.e. 0.4 to 0.8 ml/kg IP, IM).
Mice: xylazine (7.5-16 mg/kg IP) + ketamine (90-100 mg/kg IP i.e. 0.9 to 1.0 ml/kg IP).
Guinea pigs: xylazine (0.1-5 mg/kg IM) + ketamine (30-80 mg/kg IM i.e. 0.3 to 0.8 ml/kg IM).
Hamsters: xylazine (5-10 mg/kg IP) + ketamine (50-200 mg/kg IP i.e. 0.5 to 2 ml/kg IP).

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

The vial 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.

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

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.

4.11 Withdrawal period(s)

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

Not authorised for use in rabbits for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: anaesthetics, other general anaesthetics, ketamine
ATCvet code: QN01AX03

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzethonium chloride
Water for injections

6.2 Major incompatibilities

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

6.3 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.

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

Brown type I glass vials containing 10 ml, 20 ml and 50 ml 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.

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

Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

8. MARKETING AUTHORISATION NUMBER