AGENCE NATIONALE DU
MEDICAMENT VETERINAIRE

Agence nationale du médicament vétérinaire (ANMV) – French agency for veterinary medicinal products
AGENCE NATIONALE DE SÉCURITÉ SANITAIRE de l'alimentation, de l'environnement et du travail –
FRENCH AGENCY FOR FOOD, ENVIRONMENTAL AND OCCUPATIONAL HEALTH AND SAFETY
14 rue Claude Bourgelat – PA de la Grande Marche – Javené - CS 70611 – F-35306 FOUGERES Cedex
www.anses.fr — @Anses_fr

# DECENTRALISED PROCEDURE

# PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

# KETEXX 100 MG/ML SOLUTION FOR INJECTION

# DATE: 11/05/2022

# MODULE 1

## PRODUCT SUMMARY

| | |
|---|---|
| EU Procedure number | FR/V/0435/001/DC |
| Name, strength and pharmaceutical form | Ketexx 100 mg/mL solution for injection |
| Applicant | ALFASAN NEDERLAND<br>KUIPERSWEG 9<br>3449 JA WOERDEN<br>NETHERLANDS |
| Active substance(s) | Ketamine (as ketamine hydrochloride) |
| ATC Vetcode | QN01AX03 |
| Target species | Dogs, cats, cattle, sheep, goats, horses, guinea pigs, hamsters, rabbits (exclusively kept as pet), rats, mice |
| Indication for use | The product may be used in combination with a sedative for:<br>- Immobilisation<br>- Sedation<br>- General anaesthesia |

# MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website https://www.anses.fr/en/thematique/veterinary-medicine-anmv

# MODULE 3

## PUBLIC ASSESSMENT REPORT

| | |
|---|---|
| Legal basis of original application | Article 13(1) Generic application (Directive No 2001/82/EC) |
| Date of completion of the original decentralised procedure | 30 March 2022 |
| Concerned Member States for original procedure | AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NL, NO, PL, PT, RO, SE, SI, SK, UK(NI) |

## I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.
It has been shown that the product can be safely used in the target species; the adverse reactions observed are indicated in the SPC.
The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

## II. QUALITY ASPECTS

### *A. Composition*

The product contains 100 mg/ml of ketamine (as hydrochloride) as active substance and excipients benzethonium chloride and water for injections.
The packaging of the finished product is as described in the SPC. The particulars of the containers and controls performed are provided and conform to the regulation.
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

### *B. Method of Preparation of the Product*

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.
Process validation data on the product have been presented in accordance with the relevant European guidelines.

### *C. Control of Starting Materials*

The active substance is ketamine hydrochloride, an established substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.
The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

### *D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies*

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

### *E. Control on intermediate products*

Not applicable.

### *F. Control Tests on the Finished Product*

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.
Satisfactory validation data for the analytical methods have been provided.
Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

### *G. Stability*

A re-test period for the active substance is set in the certificate of suitability issued by EDQM.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.
An in-use shelf-life as detailed on the SPC has been supported by appropriate data.

## III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

### *III.A Safety Testing*

#### *Pharmacological Studies*

See Part IV.A.

#### *Toxicological Studies*

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

#### *User Safety*

The applicant has provided a user safety assessment in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

#### *Environmental Risk Assessment*

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required.

If use as recommended, the product will have a negligible environmental impact.

### *III.B Residues documentation*

### *MRLs*

The active substance, ketamine, is included in table 1 of the annex of the Commission Regulation (EU) No. 37/2010, as follows:

| Marker residue | Animal Species | MRL | Target Tissues | Other Provisions | Therapeutic Classification | Regulation |
|---|---|---|---|---|---|---|
| Not applicable | All food producing species | No MRL required | Not applicable | No entry | No entry | 37/2010 of 22.12.2009 |

In addition the following entry in the list of substances considered as not falling within the scope of Regulation No. 470/2009 applies for the excipient benzethonium chloride:

> *Benzethonium chloride (CAS 121-54-0): for use as a preservative in intravenously administered products and at concentrations of up to 0.01% resulting in target animal doses of up to 8 µg/kg bw.*

The condition is fulfilled for the proposed product.

### *Withdrawal Periods*

No depletion study was provided. This is acceptable for both the intravenous and intramuscular routes, according to the type of application, *i.e.* a generic application and the MRL status of the active substance ketamine, *i.e.* no MRL required without ADI.

## IV. CLINICAL ASSESSMENT (EFFICACY)

It is a generic application for a marketing authorisation in accordance with Article 13.1 of Directive 2001/82/EC, as amended by 2004/28/EC. The cited reference product is IMALGENE 1000 (Boehringer Ingelheim).

KETEXX 100 MG/ML SOLUTION FOR INJECTION contains ketamine. It is intended for an intravenous, intramuscular or intraperitoneal administration. The product may be used in combination with a sedative for:

- Immobilisation
- Sedation
- General anaesthesia

**Pharmaceutical form**

The generic product and the reference product have the same pharmaceutical form: solution for injection.

**Active substance qualitative and quantitative composition**

The generic and reference products have the same qualitative and quantitative composition in active substance: 100 mg of ketamine (equivalent to 115.3 mg of ketamine hydrochloride) per mL of product.

**Bioequivalence studies**
No study was performed.

The bioequivalence between the reference product, IMALGENE 1000 and the generic product KETEXX 100 MG/ML SOLUTION FOR INJECTION is accepted according to the section 7.1 of the bioequivalence (EMA/CVMP/016/2000-Rev.3).

### *IV.A Pre-Clinical Studies*

### *Pharmacology*

No data was provided to document the pharmacology part according to the legal basis of the application.

### *Tolerance in the Target Species of Animals*

The applicant has not provided tolerance study which is acceptable because:
- the generic product and the reference product are bioequivalent,
- the excipients of the generic product are deemed unproblematic as regards tolerance.

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

### *IV.B Clinical Studies*

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

## V. OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.