FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ketabel 100 mg/ml solution for injection (BG, CZ, DE, EE, EL, FR, HU, IE, LT, LV, NL, PT, RO, SK, SL and UK)
Ketabel vet. 100 mg/ml solution for injection (FI, IS, SE)
Belatamin 100 mg/ml solution for injection (AT)
Drømmetamin vet. 100 mg/ml solution for injection (NO)

Date: 12 March 2020

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0338/001/DC
Name, strength and pharmaceutical form	Bela-Pharm GmbH & Co. KG
Applicant	Bela-Pharm GmbH & Co. KG Lohner Straße 19 49377 Vechta Germany
Active substance(s)	Ketamine hydrochloride
ATC Vetcode	QN01AX03
Target species	Dogs, cats, cattle, sheep, goats, horses, pigs, guinea pigs, hamsters, rabbits, rats, and mice
Indication for use	The product may be used in combination with a sedative for: - Immobilisation - Sedation - General anaesthesia

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.anmv.anses.fr/

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	17/04/2019
Concerned Member States for original procedure	AT, CZ, EE, EL, FI, HU, IE IS, LT, LV, NL, NO, PT, RO, SE, SI, SK, UK, BG, DE

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 slight 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 ketamine (as hydrochloride) as active substance, and excipients chlorobutanol hemihydrate, propylene glycol and water for injections.
The container is a glass vials closed with a bromobutyl rubber stopper. The particulars of the container 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.

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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

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.
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.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

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III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of pharmacological studies are not required.

The pharmacological aspects of this product are identical to the reference product.

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.

The toxicological aspects of this product are identical to the reference product.

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.

Ecotoxicity

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

Residue Studies

No residue depletion study was conducted.

MRLs

a. active substances

The active substance, ketamine, is included in table 1 of the MRL regulation 37/2010, without ADI, 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

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b. excipients

The MRL status of excipients of the product KETAMIN 10% SOLUTION FOR INJECTION is indicated in the following table.

Excipient	MRL status
Chlorobutanol hemihydrate	Out of scope at concentrations up to 1%
Propylene glycol	Table 1, No MRL required for all species, with DJA of 25000 µg/kg
Water for injection	Out of scope

The composition of the product KETAMIN 10% SOLUTION FOR INJECTION is acceptable according to the European regulation 470/2009.

Withdrawal Periods

A consumer risk assessment about the propylene glycol should be provided to take into account its ADI and the problematic of injection site.

According to the withdrawal period established for the previous authorised products containing ketamine and to the precautionary principle for consumer risk, the RMS proposes “meat and offal” withdrawal periods of 1 day, even if no ADI and no MRL was established for this active substance.

The withdrawal periods should be modified as follows:

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

Pigs
Meat and offal: 1 day

With a maximum volume per injection site of 20 mL indicated in section 4.9.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

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

Pharmaceutical form
The test and the reference products have the same pharmaceutical form: solution for injection.

Active substance qualitative and quantitative composition
The test and reference products have the same qualitative and quantitative composition in active substance: 100 mg of ketamine per ml of product.

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Bioequivalence studies

No bioequivalence study was performed.

The exemptions of demonstration of bioequivalence are applied as follows

for the intravenous administration, the exemption 7.1.a is acceptable.

for the other routes of administration, *i.e*. intramuscular and peritoneal, the exemption 7.1.b is applied.

A satisfactory justification is provided about the addition of propylene glycol. It has no influence on the rate and/or extent of absorption of the active substance, ketamine.

The two products KETAMIN 10% SOLUTION FOR INJECTION and IMALGENE 1000 can be considered as bioequivalent.

Tolerance in the Target Species of Animals

The applicant has not provided tolerance study which is acceptable because:

- the tested product and the reference product are bioequivalent,
- the excipients of the tested 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.

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