Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ketavet 100 mg/ml Solution for injection for dogs, cats and horses
(UK, CY,EL, IE)

Ketaset 100 mg/ml Solution for injection for dogs, cats and horses.
(AT, BE, CZ, DE, ES, FR, HR, LU, MT, PL, PT, RO, SK)

Ketastesic Vet 100 mg/ml Solution for injection for dogs, cats and horses.
(DK, FI, IT, NO, SE, SI)

PuAR correct as of 17/04/2018 when RMS was transferred to ES. Please contact the RMS for future updates

Date Created: June 2015

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0472/001/DC
Name, strength and pharmaceutical form	Ketavet 100 mg/ml Solution for injection for dogs, cats and horses
Applicant	Zoetis UK Limited, 5th Floor, 6 St Andrew Street, London, EC4A 3AE
Active substance(s)	Ketamine
ATC Vetcode	QN01AX03
Target species	Dogs, Cats, Horses
Indication for use	The product may be used to induce anaesthesia: a) in conjunction with butorphanol and medetomidine in the dog and cat, b) in conjunction with xylazine in the dog, cat and horse, c) in conjunction with detomidine in the horse, d) in conjunction with romifidine in the horse. Based on the benefit/risk assessment performed by the veterinarian the product may be used as a sole agent for restraint and minor surgical procedures where muscle relaxation is not required in the domestic cat.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

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	19th November 2014
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain and Sweden.

I. SCIENTIFIC OVERVIEW

Ketavet Solution for injection for dogs, cats and horses has been developed as a generic of Ketaset solution for injection. The reference product has been authorised in the UK since April 1990. The application is for a generic product as bioequivalence could be demonstrated.

The product contains 100 mg/ml of ketamine (as hydrochloride) to be administered via injection at a dose rate of 1.1 -33 mg ketamine/kg bodyweight, depending on the species and other agents being used. The product is indicated to induce anaesthesia:

a) in conjunction with butorphanol and medetomidine in the dog and cat,

b) in conjunction with xylazine in the dog, cat and horse,

c) in conjunction with detomidine in the horse,

d) in conjunction with romifidine in the horse.

Based on the benefit/risk assessment performed by the veterinarian the product may be used as a sole agent for restraint and minor surgical procedures where muscle relaxation is not required in the domestic cat.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species and any reactions observed are indicated in the SPC.[1]

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 [2] of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains ketamine (as hydrochloride) as the active substance. The excipients used are benzethonium chloride and water for injections.

The container/closure system consists of a clear, colourless Type I glass vial sealed with a chlorobutyl stopper and aluminium flip off cap as either a 10 ml or 50 ml pack size. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservative are justified. The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

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.

II.C. Control of Starting Materials

The active substance is ketamine hydrochloride, an established active 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.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

The excipients described in a pharmacopeia are manufactured in accordance with the relevant Ph. Eur. monographs. Certificates of analysis were provided for both excipients.

II.C.4. Substances of Biological Origin

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

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. 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. The tests include those for identification and assay of the active substance and excipients, appearance and sterility.

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.

II.F. Stability

Stability data on the active substance has 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. Data were provided for batches stored at 25ºC/60%RH, 30ºC/60%RH and 40ºC/75%RH, in accordance with VICH guidelines. The data support a shelf life of 2 years.

In-use stability studies were also submitted. A 50ml vial was punctured 20 times and 50% of the product removed on day 0. The batch was tested for stability and the vial was stored at 25°C/60%RH for 28 days. An in-use shelf life of 28 days has been established.

G. Other Information

Shelf life

- Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
- Shelf life after first opening the immediate packaging: 28 days.

Special precautions for storage

- No special temperature storage conditions are required.
- Store in the original container in order to protect from light.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 .(1), and bioequivalence with a reference product has been established, results of pharmacological and toxicological tests are not required.

Warnings and precautions as listed on the product literature are more extensive than those of the reference product and are adequate to ensure safety of the product to users and the environment.

III.A Safety Documentation

User Safety

The applicant has provided a user risk assessment in compliance with the relevant guideline. The SPC carries the following warnings and precautions to ensure safety to users of the product. No further assessment was required:

- This is a potent drug. Particular care should be taken to avoid accidental self-administration.
- Preferably use a guarded needle until the moment of injection.
- People with known hypersensitivity to ketamine should avoid contact with the product.
- Avoid contact with the skin and eyes. Wash any splashes from skin and eyes immediately with large amounts of water.
- In case of accidental self-injection, or if symptoms occur after ocular/oral contact, seek medical advice immediately and show the package leaflet or the label to the physician, but DO NOT DRIVE.
- Adverse effects on the foetus cannot be excluded. Pregnant women should avoid handling the product.
- Advice to doctors:

  Do not leave patient unattended. Maintain airways and give symptomatic and supportive treatment.

Environmental Safety

The applicant provided a Phase I environmental risk assessment in compliance with the relevant guidelines which showed that no further assessment is required. The assessment concluded that the product will be used in a small

number of animals and is not expected to pose a risk to the environment when used as recommended.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because the applicant has demonstrated the product is formulated and manufactured in the same way as the reference product so the following withdrawal periods apply.

Withdrawal period
Horses (meat and offal): 1 day
(milk): 1 day

IV CLINICAL DOCUMENTATION

As this was a generic application according to Article 13. (1) and bioequivalence with a reference product has been established, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.I. Pre-Clinical Studies

As this was a generic application according to Article 13. (1) and bioequivalence with a reference product has been established, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.II. Clinical Documentation

As this was a generic application according to Article 13. (1) and bioequivalence with a reference product has been established, 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 benefit/risk profile of the product(s) is favourable

.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)