FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS AGENCE NATIONALE DU MEDICAMENT VETERINAIRE
8 rue Claude Bourgelat –
Parc d'activités de la grande Marche –
Javené – CS 70611 – 35306
FOUGERES

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Pracetam 40% solution buvable pour porc (FR)

Pracetam 400 mg/ml solution for use in drinking water for pigs

Pracetam Vet 400 mg/ml solution for use in drinking water for pigs (DK)

DATE : 17/06/2016

French agency for food, environnemental and occupational health safety– French Agency for Veterinary Medicinal Products
8 rue Claude Bourgelat – Parc d'activités de la grande Marche – Javené – CS 70611 – 35306 FOUGERES - Téléphone : + 33 (0)2 99 94 78 78 - Télécopie : + 33 (0)2 99 94 78 60 - www.anses.fr

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0181/002/MR
Name, strength and pharmaceutical form	Pracetam 40% solution for use in drinking water for pigs
Applicant	CEVA SANTE ANIMALE 10 avenue de la Ballastière 33500 LIBOURNE
Active substance(s)	Paracetamol
ATC Vetcode	QN02BE01
Target species	Pigs
Indication for use	Symptomatic treatment of fever in the context of respiratory diseases in combination with an appropriate anti infective therapy, if necessary

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Extension to an existing marketing authorisation in accordance with Article 12 (3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition	28/04/2016
Date product first authorised in the Reference Member State (MRP only)	20/12/2005
Concerned Member States for original procedure	AT, BE, BG, CZ, DE, DK, EE, ES, HU, IT, LT, LV, NL, PL, PT, RO, SK, UK

I. SCIENTIFIC OVERVIEW

For public assessment reports for the first authorisation in a range:

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 400 mg/ml paracetamol and dimethyl sulfoxide, Ponceau 4R, and Macrogol 300 as excipients.

The product is packed as detailed 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 paracetamol, 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.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

The product is an extension of the previous marketing authorisation for Pracetam 20% and is an addition of a new strength. Bioequivalence of the product with the reference product can be assumed and pharmacology of the active substance has previously been addressed for this product. Cross reference is made to this data and no further data is required.

Toxicological Studies

Bioequivalence of the product with the reference product, Pracetam 20%, can be assumed and toxicology of the active substance has previously been addressed for this product. Cross reference is made to this data and no further data is 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.

Ecotoxicity

The applicant has provided a phase I and phase II environmental risk assessment in compliance with the relevant guideline

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted since the test product is assumed and accepted to be bioequivalent to the reference product and the product is administered via oral route at the same dosage regimen as the one of the reference product.

MRLs

a. active substances

The active substance, paracetamol, is included in table 1 of the MRL regulation 37/2010, as follows,

Marker residue	Animal Species	MRL	Target Tissues	Other Provisions	Therapeutic Classification
Not applicable	Porcines	No MRL required	Not applicable	For oral use only	No entry

b. excipients

The MRL status of excipients of the product Pracetam 40% solution for use indrinking water for pigs is indicated in the following table.

Excipients	MRL status
E124 85%	No MRL required
Dimethylsulfoxyde	No MRL required
Macrogol 300	No MRL required

Withdrawal Periods

Since the bioequivalence with the reference product has been demonstrated, the withdrawal periods retained are identical to those authorised for the reference product:

Species	Tissues	Withdrawal periods
Pig	Meat & offal	Zero days

IV. CLINICAL ASSESSMENT (EFFICACY)

Tolerance in the Target Species of Animals

Because of the presence of Dimethylsulfoxyde, the applicant has conducted a GCP[1] reprotoxicity study in sow during pregnancy and lactation in compliance with the relevant guideline. The results of this reproductive study shows the good tolerance of the product when orally administered to sows at different reproductive stages and demonstrates that PRACETAM 40% did not induce adverse effects when administered to pregnant and lactating sows.

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

IV.B Clinical Studies

The applicant conducted suitable *in vivo* bioequivalence study between the two formulations Pracetam 40% and Pracetam 20%. As a result the bioequivalence has been satisfactorily demonstrated.
On the basis of this *in vivo* bioequivalence study between the test and the reference product, the results of the clinical studies previously performed on Pracetam 20% can be extrapolated to Pracetam 40% and no further data is required.

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

[1] Good Clinical Practice

for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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 veterinary Heads of Agencies website (www.HEVRA.org).

This section 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.

<None>

or

Complete this section for extensions to the same VPA range or defined, significant variations, using the table shown below.

Some examples of significant changes in safety or efficacy data are:

- *Changes to pharmacokinetic data leading to a change in the SPC*
- *Changes to toxicological data leading to a change in the SPC*
- *Changes to user safety warnings*
- *Changes to ecotoxicological information as given in the SPC or changes to disposal warnings*
- *New residue studies in new target species or tissues*
- *Reassessment of residue data or new studies resulting from changes to MRL*
- *Changes to withdrawal period*
- *Changes to target species*
- *Changes to target species tolerance data leading to change in warnings/precautions for target species*
- *New or changed indications*

Significant changes in administrative or quality data include any Type II change, which affects the initial report. The following Type IA or IB changes may also apply:

- *Name of product [Type IA: 2]*
- *Name of active substance [Type IA: 3}*
- *MAH [Type IA: 1]*
- *Composition of the medicinal product [Type IB: 18, Type IA/B: 25, 34, 35, 39]*
- *Container/closure system [Type 1/B: 26, 28, 29, 36, 41, 43]*
- *Method of preparation [Type 1B: 33]*
- *Active substance specification [Type IB: 25]*
- *CEP [Type IA/B: 15]*
- *Re-test period or storage conditions of active substance [Type IB: 17]*
- *Excipient specifications [Type 1A/B: 25]*
- *Packaging materials[Type 1A/B: 28, 29, 36, 41, 43]*
- *TSE [Type 1A: 16, 22]*

- *Shelf-life or storage conditions of the finished product [Type 1B: 42]*

Quality changes

Summary of change (Application number)	**Section updated in Module 3**	**Approval date**
<Example: Change to active substance specification> (MS/V/XXX/X/IB/XX)	N/A	

Safety/efficacy changes

Summary of change (Type; application number)	**Section updated in Module 3**	**Approval date**
<Example: Addition of target species - pigs> (MS/V/XXX/X/II/XX)	<IIIA> <IIIB> <IV>	