College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500 3531 AH Utrecht The Netherlands

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Furosoral 10 mg tablets for cats and dogs Furosoral 40 mg tablets for cats and dogs

Created: December 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0192/001-002/MR
Name, strength and pharmaceutical form	Furosoral 10 mg tablets for cats and dogs Furosoral 40 mg tablets for cats and dogs
Applicant	AST Farma B.V. Wilgenweg 7 3421 TV Oudewater Nederland
Active substance(s)	Furosemide
ATC Vetcode	QC03CA01
Target species	Cats and dogs
Indication for use	Treatment of hydrothorax, hydropericardium, ascites and oedema, particularly associated with cardiac insufficiency and renal dysfunction.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended for Furosoral 10 mg tablets for cats and dogs. Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended for Furosoral 40 mg tablets for cats and dogs.
Date of completion of the original mutual recognition procedure	24 September 2014
Date product first authorised in the Reference Member State (MRP only)	7 September 1998
Concerned Member States for original procedure	AT, BE, CY, CZ, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK.
Concerned Member States for Repeat Use procedure	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 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.

Furosoral is a generic/hybrid application. The reference product is Dimazon 40 mg tabletten voor honden en katten (Intervet NL, REG NL 5285), registered in the Netherlands since 1992. The initial application for Dimazon 40 mg tabletten voor honden en katten was assessed before there was a requirement to have a public assessment report; therefore no details in this section are available.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The tablets contain 10 mg or 40 mg furosemide and the following core excipients:

lactose monohydrate, maize starch, microcrystalline cellulose, povidone (K25), crospovidone, purified talc,

pregelatinized starch, silicon dioxide and longchained partial glycerides.

The tablet is cross scored and meant to be broken in halves or quarters.

The products are packed in PVC/PVDC-Al blisters, each containing 10 tablets.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

A bioequivalence study has been done with 40 mg tablets against Dimazon 40 mg tablets.

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.

The product is manufactured using conventional manufacturing techniques. However, suitable pre-approval validation results on three production scale batches of both tablet strengths have been provided. The tests performed during production are described.

C. Control of Starting Materials

The active substance furosemide is an established active substance described in the European Pharmacopoeia. The active substance is manufactured at IPCA Laboratories Limited in accordance with the principles of good manufacturing practice.

The CEP procedure has been employed.

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.

Silicon dioxide and longchained partial glycerides (not described in the Ph.Eur.) comply with the requirements of the DAB. All other excipients are in conformity with the Ph.Eur. requirements.

The packaging is conformity with the Ph Eur and EU Food Directive. However, a statement should be provided that the heat seal laquer LX4DP complies *EU Regulation 10/2011 relating to plastic materials and articles intended to come into contact with food*.

There are no substances of biological origin within used in the manufacture of this product.

D. Control on intermediate products

Not applicable.

E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. Most tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. The dissolution limit needs reconsideration.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical

data from the proposed production site has been provided demonstrating compliance with the specification.

F. Stability

The retest period of 5 years of the active substance when stored under the approved conditions is evidenced by the CEP.
Stability data on the finished product have been provided in accordance with applicable VICH guidelines. According to the stability results provided the claimed shelf life of 36 months can be granted for both Furosoral 10 and 40 mg tablets.

G. Other Information

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

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

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that hypersensitivity reactions may occur to the active substance or the excipients.
Warnings listed on the product literature are:
"Furosemide has possible genotoxic properties and there is evidence of carcinogenicity in mice. Although there is inadequate evidence relating to these effects in humans, skin contact with or accidental ingestion of the product should be avoided. Wear impervious gloves during handling and administration of the product and wash hands thoroughly afterwards. Each time an unused part-tablet is stored until next use, it should be returned to the open blister space and inserted back into the cardboard box. The product should be stored safely, out of the sight and reach of children. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

People with known hypersensitivity to furosemide and other ingredients in the product should avoid contact with the veterinary medicinal product. Do not handle this product if you know you are sensitive to sulphonamides as hypersensitivity to sulphonamides may lead to hypersensitivity to furosemide. If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention. Wash hands after use."

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

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines. The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will only be used in nonfood animals.

IV. CLINICAL ASSESSMENT (EFFICACY)

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.

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 Heads of Veterinary Medicines Agencies website (www.HMA.eu).

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.

Summary of change	**Section updated**	**Approval date**
Addition of a site for secondary packaging and batch-release (NL/V/0192/IA/001-002/G).	N/A	8 February 2015
Change in the invented name of the veterinary medicinal product from Furosoral vet to Furosoral in Poland. (NL/V/0192/001-002/IB/002)	N/A	31 December 2016
Transfer of MAH from AST Beheer B.V. to AST Farma B.V (National procedure)	N/A	May 2015
Renewal (NL/V/0192/001-002/R/001)	N/A	28 May 2019
Introduction of a new pharmacovigilance system. (NL/V/xxx/WS/021)	N/A	12 July 2019
Repeat Use Procedure (CMS: DE) (NL/V/0192/001-002/E/001)	Module 3	23 October 2019