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

Nytox 1000 mg/g Powder for Solution for Fish Treatment

Date Created: 13th December 2016

PuAR correct as of 27/02/2019 when RMS was transferred to NO.
Please contact the RMS for future updates.

Updated: December 2017

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0584/001/DC
Name, strength and pharmaceutical form	Nytox 1000 mg/g Powder for Solution for Fish Treatment
Applicant	NAQUA Ltd Unit 8 Starborough Farm Starborough Road Nr Edenbridge Kent TN8 5RB
Active substance(s)	Tricaine methanesulfonate
ATC Vetcode	QN01AX93
Target species	Ornamental fish, or their development stages, and breeding and juvenile stages of fish.
Indication for use	For use in an immersion bath for sedation, immobilisation and anaesthesia of fish for: vaccination, transportation, weighing, tagging, clipping, stripping of breed stock, blood-sampling and surgical procedures.

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	06/10/2016
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Norway

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, submitted in accordance with Article 13 (1) of Directive EC 2001/82/EC as amended. The reference product is MS222 100% w/w Powder for Solution for Fish Treatment authorised in the UK since September 1992. Bioequivalence was accepted based on 7.1.d) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2) as the product is identical in formulation to the reference product.

The target species are ornamental fish, or their development stages, and breeding and juvenile stages of fish. The product is indicated for use in an immersion bath for sedation, immobilisation and anaesthesia of fish for vaccination, transportation, weighing, tagging, clipping, stripping of breed stock, blood-sampling and surgical procedures. The product should be dissolved in water of the same composition and characteristics to that which the fish are accustomed to form an aqueous solution. The safety and efficacy of the product are influenced by a number of factors such as concentration of the drug in water, duration of exposure, temperature, oxygen and density of biomass and therefore the amount to be administered is variable. It is recommended that a test of the selected drug concentration and exposure time is conducted with a small group of representative fish before treating large numbers. For further information on the amounts to be administered, please refer to Section 4.9 of the SPC[1].

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, any reactions observed are indicated in the SPC.[1] 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 [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 1g of tricaine methanesulphonate 1g, there are no excipients. The container/closure system consists of high density polyethylene tamper resistant bottles closed with an integral, tamper evident, low density polyethylene cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence 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. The manufacturing method consists of sieving the active substance, filling the container and labelling

The product is manufactured using straightforward and conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation based on a check of the uniformity of fill weights and torque setting on cap assembly.

II.C. Control of Starting Materials

The active substance is tricaine methanesulphonate, an established active substance, and is manufactured in accordance with the principles of good manufacturing practice.

The active substance is manufactured in accordance with an ASMF[3]. The specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

There are no excipients in this product.

[2] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.
[3] ASMF – Active Substance Master File.

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.

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. Control tests on the finished product include those for appearance, identification, degradation products, minimum fill and moisture content.

II.F. Stability

Stability data on the active substance have been provided within the ASMF, demonstrating the stability of the active substance when stored under the approved conditions. A re-test period for the active substance of 60 months when stored in the commercial packaging is acceptable.

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.
The claim of a 12 hour stability after dilution or reconstitution is based on information from the reference product.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 30 months
Shelf life after dilution or reconstitution according to directions: 12 hours

<u>Special precautions for storage:</u>
Store in a dry place.
Store in the original container.
Keep the container tightly closed in order to protect from moisture.
Protect solution from direct sunlight.

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 the same as those of the reference product and are adequate to ensure safety of the product to users, the environment, and to consumers.

III.A Safety Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline which claims that as the product is identical in formulation to the reference product, the same extensive user safety warnings could be used for this product. This is considered acceptable. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Safety

A Phase I environmental risk assessment (ERA) in line with the relevant VICH guideline (CVMP/VICH/592/98-FINAL) was submitted. At Question 11 of the VICH decision tree the applicant has stated that the $EIC_{aquatic}$ of the product released from aquaculture facilities is less than 1 µg/l. When calculating the estimate of environmental exposure, the applicant used the reasonable worst case scenario of 100 mg/l which is the maximum concentration used for Atlantic salmon, a major food producing species. Although the maximum use rate of 200 mg/l for use with carp is indicated, carp are considered a minor species under Question 4 of the VICH decision tree, with environmental exposure being low. Therefore the worst case scenario is acceptable. A Phase II assessment was not required.

III.B.2 Residues documentation

Residue Studies

As essential similarity to the reference product has been accepted, no residues depletion studies have been provided, which is acceptable. The proposed methods of administration and dosage regime for use in the food producing target species are identical to the reference product and therefore, the same withdrawal period is proposed and considered acceptable.

MRLs

Tricaine methanesulphonate is listed in Table 1 of Regulation (EU) No. 37/2010 with no MRL required for fish meat.

Withdrawal Periods

Based on the data provided, a withdrawal period of 70 degree days after the end of treatment is justified. Fish must not be slaughtered for human consumption during treatment.

IV CLINICAL DOCUMENTATION

As this is a generic application according to Article 13 (1) and bioequivalence with a reference product has been established on the basis of being of identical formulation to the reference product (7.1.d) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2)), 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)