ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Tricaine Pharmaq 1000 mg/g Powder for Solution for Fish Treatment

PuAR correct as of 26/11/2018 when RMS was transferred to NO.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0405/001/DC
Name, strength and pharmaceutical form	Tricaine Pharmaq 1000 mg/g Powder for Solution for Fish Treatment
Applicant	Pharmaq Limited Unit 15 Sandleheath Industrial Estate Fordingbridge Hampshire SP6 1PA United Kingdom
Active substance	Tricaine methane sulphonate
ATC Vetcode	QN01AX93
Target species	1) Ornamental fish, or their development stages, and 2) 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 Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

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	21st November 2012.
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Greece, Iceland, Ireland, Italy, Norway, Spain.

I. SCIENTIFIC OVERVIEW

This was a generic application for Tricaine Pharmaq 1000 mg/g Powder for Solution for Fish Treatment, submitted in accordance with Article 13 (1) of Directive 2001/82/EC as amended. The reference product was MS222 100% w/w Powder for Solution for Fish Treatment, first authorised in the UK in September 1992. Bioequivalence was claimed with the reference product on the grounds of identical similarity. The product may be used to sedate, immobilise and anaesthetise fish of ornamental and food-producing species, via immersion. The concentration of product used may vary with the level of anaesthesia required, and the species of fish being treated.

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.[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 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.

[1] SPC – Summary of Product Characteristics.

II. QUALITY ASPECTS

A. Composition

The product contains tricaine methane sulphonate. There are no excipients.

The container/closure system consists of High Density Polyethylene (HDPE) tamper resistant tubs closed with and integral, tamper evident, low density polyethylene cap (snap on) or polypropylene screw cap containing 25 g, 100 g, 250 g or 1000 g of product. 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.

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 tricaine methane sulphonate, an established active substance which is not described in the European Veterinary 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

A declaration was provided, in compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products stating that 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. A variety of appropriate stability tests were performed on the finished product.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after dilution or reconstitution according to directions: 24 hours.

Store in the original container.
Store in a dry place.
Keep the container tightly closed in order to protect from moisture.
Protect from direct sunlight.
This veterinary medicinal product does not require any special temperature storage conditions.

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 pharmacological and toxicological tests are not required. A User Risk Assessment and Environmental Risk Assessment were provided.

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 consumers.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in the form of references, in compliance with the relevant guideline which shows that as the product is to be administered by veterinary surgeons, there is low risk to others. Possible routes of exposure to users are via the dermal, ocular or oral routes. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. The SPC carries the following warnings:-

- 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 Tricaine mesilate (Tricaine methanesulfonate) should avoid contact with the veterinary medicinal product.
- Personal protective equipment consisting of impermeable rubber gloves should be worn when handling the veterinary medicinal product.
- Do not create dust when handling the powder or preparing the anaesthetic solution. In case of accidental inhalation of dust, move to fresh air and if breathing is affected, seek medical advice immediately and show the doctor the product label. In situations where dust is created when handling the powder, wear a disposable half mask respirator conforming to European Standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143.
- Avoid contact with skin and eyes. In case of accidental contact, immediately wash the affected area with plenty of clean running water. If irritation persists, seek medical advice.
- Do not eat, drink or smoke whilst handling this product.
- Wash hands after use.

Ecotoxicity

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 required because the product was considered identical to the reference product.

Withdrawal Periods

- Fish must not be slaughtered for human consumption during treatment.

- Fish can only be harvested for human consumption 70 degree days after the last treatment.

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.

IV.A Pre-Clinical Studies

Pharmacology

The SPC carries the appropriate pharmacodynamic and pharmacokinetic information.

Pharmacodynamics

The active substance has similar properties to ester and amide anaesthetics. It is more water-soluble than benzocaine, which recommends it for use in this instance. During immersion, fish absorb and excrete the product via the gill epithelium. The product causes a reduced blood flow through the gills, leading to reduced oxygen consumption. Concentration and water temperature will have an effect on rate of narcosis, with higher temperatures causing a greater narcotic effect, but with less of a safety margin. If fish are placed in non-medicated water, the narcotic effect is reversed.

Pharmacokinetics

The solubility of the active substance in lipids may accounts for rapid diffusion across the gills. The product is distributed throughout the body. Excretion occurs mainly via the gills and to some extent the kidneys. All species appear to produce an acetylated derivative, usually amounting to less than 20% of the original active substance. Kidney excretion may vary between species, but efficacy varies between species due to free movement across the gills. In salmonids, the concentration in muscle ranges from 9.4 72.0 mg/kg, with a half-life on withdrawal of approximately 70 minutes. 24 hours therefore equates to 20 half lives. Highest concentration of the product discovered in salmonid muscle after 24 hours were seen to be 2.6 to 3.2 mg/kg.

Tolerance in the Target Species of Animals

As this was a generic application, and bioequivalence was successfully claimed, there was no requirement for data in this section. The SPC carries appropriate information.

Resistance

As this was a generic application, and bioequivalence was successfully claimed, there was no requirement for data in this section. The SPC carries appropriate information.

IV.B Clinical Studies

Laboratory Trials

As this was a generic application, and bioequivalence was successfully claimed, there was no requirement for data in this section.

Field Trials

As this was a generic application, and bioequivalence was successfully claimed, there was no requirement for data in this section.

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 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 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)