Date of Index Listing: December 20, 2024

FREEDOM OF INFORMATION SUMMARY

ORIGINAL REQUEST FOR ADDITION TO THE INDEX OF LEGALLY MARKETED UNAPPROVED NEW ANIMAL DRUGS FOR MINOR SPECIES

MIF 900-042

Faunamor

(methylthionine chloride, malachite green oxalate, acriflavine chloride immersion solution)

Ornamental finfish

For the treatment of *Ichthyophthirius multifiliis* (white spot disease) and the associated bacterial infections in ornamental finfish

Requested by:

Aquarium Münster Pahlsmeier GmbH

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I. GENERAL INFORMATION

A. File Number

MIF 900-042

B. Requestor

Aquarium Münster Pahlsmeier GmbH
Galgheide 8
Telgte, 48291, GM

U.S. Agent Name and Address:

Mr. Louis Ekus
Secretary
Aquarium Münster USA, Inc.
44 Center Street
Montague, MA 01351

C. Proprietary Name

Faunamor

D. Drug Product Established Name

methylthionine chloride, malachite green oxalate, acriflavine chloride immersion solution

E. Pharmacological Category

Antiparasitic/antimicrobial

F. Dosage Form

Immersion solution

G. Amount of Active Ingredient

2.5 mg/mL methylthionine chloride
1 mg/mL malachite green oxalate
0.3 mg/mL acriflavine chloride

H. How Supplied

20 mL and 100 mL (glass) bottles

I. Dispensing Status

Over the counter (OTC)

J. Dosage Regimen

1 mL of Faunamor per 100 L of aquarium water for three doses (Day 1, Day 2, and Day 7); for severe infestations, double the dosage to 2 mL of Faunamor per 100 L of aquarium water for three doses (Day 1, Day 2, and Day 7).

K. Route of Administration

Immersion

L. Species/Class

Ornamental finfish

M. Indication

For the treatment of *Ichthyophthirius multifiliis* (white spot disease) and the associated bacterial infections in ornamental finfish

II. EFFECTIVENESS AND TARGET ANIMAL SAFETY

In accordance with 21 CFR part 516, a qualified expert panel evaluated the target animal safety and effectiveness of Faunamor for the treatment of *Ichthyophthirius multifiliis* (white spot disease) and the associated bacterial infections in ornamental finfish and determined whether the benefits of using Faunamor for the proposed use outweigh its risks to the target animals. FDA found the members of the qualified expert panel acceptable as per 21 CFR 516.141(b). The members of the qualified expert panel were:

- James D. Bowker, M.S. - Panel Leader
- Shane W. Ramee, Ph.D.
- Timothy J. Bruce, Ph.D.

A. Findings of the Qualified Expert Panel

The qualified expert panel performed a comprehensive review of available literature, study reports from Aquarium Münster, and information supporting effectiveness of each of Faunamor's active ingredients. Additionally, they used anecdotal information and their own expertise in fish health to complete their assessment of the target animal safety and effectiveness of Faunamor in ornamental finfish.

An effectiveness study conducted by Aquarium Münster demonstrated that Faunamor effectively eliminates or significantly reduces infestations of *Ichthyophthirius multifiliis* on 19 different fish species that were heavily infested with the parasite. Similarly, a safety study conducted by Aquarium Münster on 23 different species of fish showed a margin of safety that is likely close to 4x the recommended treatment dose, as evidenced by the presence of no mortality at the 2x dose and very low mortality at the 4x dose. Several individuals with many years of experience using Faunamor in the commercial ornamental fish sector provided testimonials in which they all agreed that the product effectively controls parasite infestations that cause white spot disease in a wide range of ornamental fish species.

The qualified expert panel also reviewed two studies from the published literature in which Faunamor was used to maintain healthy fish for the duration of each study. Because the objective of the studies was not to evaluate the effectiveness of this drug, information regarding effectiveness of Faunamor was not reported specifically in these studies.

Information found in peer-reviewed literature for each of the individual active ingredients of Faunamor indicated that the LC_{50} concentrations (to determine fish safety) and the concentrations needed to effectively kill *I. multifiliis* (tomonts, theronts, and/or adults) were higher for each individual active ingredient than the concentration of those same components in the combined Faunamor formulation. Similarly, the recommended dosages of commercial single active ingredient aquarium products available online are comparable to the concentrations reported in the peer-reviewed literature. Thus, the concentrations of the three active ingredients in Faunamor, effective in controlling white spot disease, are less than the typical concentration of those same active ingredients when each is used on its own. According to the literature, the primary target pathogens of malachite green oxalate appear to be common parasites and protozoans, most notably, *I. multifiliis*. Secondary and tertiary target pathogen appear to be fungal infections and marine ich (*Cryptocaryon irritans*), respectively. The primary target pathogen of methylthionine chloride appears to be fungus, with external protozoans, such as *I. multifiliis,* being secondary targets. In contrast, acriflavine appears to be a broader spectrum product and targets external bacteria such as *Flavobacterium columnare*, along with a wide array of fungal and protozoal pathogens, including *I. multifiliis*.

Based on a thorough review of the literature, anecdotal information, and expert opinion, the qualified expert panel unanimously concluded that the benefits of using Faunamor for the treatment of *Ichthyophthirius multifiliis* (white spot disease) and the associated bacterial infections in ornamental finfish outweigh the risks to the target animals. The panel also recommended that Faunamor should be made available Over the counter (OTC).

B. Literature Considered by the Qualified Expert Panel

1. Antychowicz J. 1997. The influence of some chemical compounds upon the development of *Ichthyophthirius multifiliis*. Bulletin of the Veterinary Institute in Pulawy. 21:35-43.
2. Abou-Okada M, AbuBakr J0, Hassan A, Abdel-Radi S, Aljuarydi SH, Abdelsalam M, Taho E, Younis NA, and Abfel-Moneam DA. 2021. Efficacy of Acriflavine for controlling parasitic diseases in farmed Nile tilapia with emphasis on fish health, gene expression analysis, oxidative stress, and histopathological alterations. Aquaculture. 541:1-10.
3. Buchmann, K, Jensen PB, and Kruse KD. 2003. Effects of sodium percarbonate and garlic extract on *Ichthyophthirius multifiiiis* theronts and tomocytsts: In vitro experiments. North American Journal of Aquaculture. 65:21-24.
4. Chambel, J, Costa R, Gomes M, Mendes S, Baptista T, and Pedrosa R. 2014. Hydrogen peroxide, iodine solution and methylene solution highly enhance the hatching rate of freshwater ornamental fish species. Aquaculture International. 22:1743-1751.

5. Guest WC. 1983. Control of *Ichthyophthirius* in Peacock Bass fingerlings. Progressive Fish Culturist. 45:57.
6. Leteux F and Meyer FP. 1972. Mixtures of malachite green and formalin for controlling *Ichthyophthirius* and other protozoan parasites offish. Progressive Fish Culturist. 34:21-26.
7. Matthews RA. 2005. *Ichthyophthirius multifiliis* Fouquet and Ichthyopthiriosis in freshwater teleost. Advances in Parasitology. 59:160-241.
8. Milinski M and Bakker TCM. 1990. Female sticklebacks use male coloration in mate choice and hence avoid parasitized males. Nature. 334: 330-333.
9. Park I-S, Baek S-W, and Moon KH. 2019. The sterilization effect of methylene blue, formalin, and iodine on egg and adult stage of Marine Medaka, *Oryzias dancena*. Development and Reproduction. 23:199-211.
10. Peters A and Michiels NK. 1996. Evidence for lack of inbreeding avoidance by selective mating in simultaneous hermaphrodite. Invertebrate Biology. 115: 99-103.
11. Tieman DM and Goodwin AE. 2001. Treatments for Ich infestations in Channel Catfish evaluated under static and flow-through water conditions. North American Journal of Aquaculture. 63:293-299.
12. Wahli T, Schmitt M, and Meier W. 1993. Evaluation of alternatives to malachite green oxalate as a therapeutant for ichthyophthiriosis in rainbow trout Oncorhynchus mykiss. Journal of Applied Ichthyology. 9:237-249.
13. Whitney-Smith W and Hoyt A. 1942. Action of Alkaline Acriflavine Solution on *Bacterium salmonicida* and Trout Eggs. Experimental Biology and Medicine. Vol 51, Issue 3.
14. Xu D-H, Zhang Q-Z, and Zhang D. 2016. Two in vitro methods for screening potential parasiticides against *Ichthyophthirius multifiliis* using *Tetrahymena thermophila*. Journal of Fish Diseases. 36:285-294.

III. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Faunamor:

User Safety Warnings:
Not for use in humans. Keep out of reach of children.

Use in a well-ventilated area. Avoid inhalation or contact with eyes or skin. Wear gloves, protective clothing, and eyewear when using Faunamor.

May be harmful if ingested. If the person is conscious, wash out mouth with copious amounts of water. Seek medical advice immediately and show the package insert or carton to the physician.

In case of contact with eyes, flush with copious amounts of water for at least 15 minutes. Remove contact lenses if present and continue rinsing. Contact emergency medical help.

In case of contact with skin, wash area immediately with copious amount of water for at least 15 minutes.

Pregnant women, women who may become pregnant, and nursing women should not handle Faunamor.

IV. AGENCY CONCLUSIONS

The information submitted in support of this request for Faunamor to be added to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (Index) for the treatment of *Ichthyophthirius multifiliis* (white spot disease) and the associated bacterial infections in ornamental finfish satisfies the requirements of section 572 of the Federal Food, Drug, and Cosmetic Act and 21 CFR part 516:

A. Determination of Eligibility for Indexing

As part of the determination of eligibility for inclusion in the Index, FDA determined that the drug for this intended use in ornamental finfish was safe to the user, did not individually or cumulatively have a significant effect on the human environment, and that the description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packaging of the new animal drug was sufficient to demonstrate that the requestor has established appropriate specifications for the manufacture of the new animal drug. Additionally, the requestor has committed to manufacture the drug in accordance with current good manufacturing practices (CGMP).

The Index is only available for new animal drugs intended for use in minor species for which there is a reasonable certainty that the animal or edible products from the animal will not be consumed by humans or food-producing animals and for new animal drugs intended for use only in a hatchery, tank, pond, or other similar contained man-made structure in an early, non-food life stage of a food-producing minor species, where safety for humans is demonstrated in accordance with the standard of section 512(d) of the act. Because this new animal drug is not intended for use in food-producing animals, FDA did not require data pertaining to drug residues in food (i.e., human food safety) for granting this request for addition to the Index.

B. Qualified Expert Panel

The qualified expert panel for Faunamor met the selection criteria listed in 21 CFR 516.141(b). The panel satisfactorily completed its responsibilities in accordance with 21 CFR part 516 in determining the target animal safety and effectiveness of Faunamor for the treatment of *Ichthyophthirius multifiliis* (white spot disease) and the associated bacterial infections in ornamental finfish.

C. Marketing Status

Faunamor will be marketed Over the counter (OTC).

D. Exclusivity

Products listed in the Index do not qualify for exclusive marketing rights.