MEDICINAL PRODUCTS FOR FARMED FISH

VETHELLAS S.A.

Vethellas is a Greek veterinary pharmaceutical company, established in 1986 with up-to-date GMP production facilities, located in the industrial area of Larissa, Greece.

Vethellas produces a range of veterinary antimicrobial products widely used in livestock farming across the EU and third countries.

Furthermore, Vethellas specializes in the production of a wide range of VMPs intended for use in the fish farming sector, which includes several broad-spectrum antimicrobial and antiparasitic products. The company, looking to the future, is operating and investing systematically, in the context of a strategic orientation to support the fish farming sector, to further expand its portfolio of fish VMPs by launching new and advanced antimicrobial and antiparasitic products.

ANTIMICROBIAL PRODUCTS FOR FARMED FISH

Vethellas produces the following antimicrobial products, which have been successfully used in the field for the treatment and control of bacterial disease conditions in farmed fish, either according to the indications of the SPCs or by derogation (cascade) provisions:

Products

1. **OXYTETRACYCLINE 50% VETHELLAS**
2. **OXYTETRACYCLINE 100% VETHELLAS**
3. **TRIMETHOPRIM-SULPHADIAZINE 50% VETHELLAS**
4. **LINACIVET® (50% OXOLINIC ACID)**
5. **SPECLIN® (50% FLORFENICOL)**

They all come in the form of premixes for incorporation into the feed.

Indications

- Pasteurellosis (*Photobacterium damselae*)
- Vibriosis (*Listonella anguillarum*, *Vibrio spp*.)
- Furunculosis/Aeromonosis (*Aeromonas spp*.)
- Freshwater and seawater Columnaris disease (*Flexibacter* and *Tenacibaculum spp*.)
- Enteric Red-Mouth disease (*Yersinia ruckeri*)

PRODUCT RANGE VERSATILITY

The above range of antimicrobial VMPs includes Oxytetracycline hydrochloride in two different concentrations (offering flexibility to select the appropriate dosage depending on fish size and season), a potentiated sulfonamide, a first-generation quinolone and an amphenicol. This versatile range enables veterinarians and fish farmers to select the most appropriate treatment solution depending on the bacterial pathogen and its sensitivity profile, ensuring targeted and effective disease management.

ANTIPARASITIC PRODUCTS FOR FARMED FISH

Vethellas produces PRAZIVETIN®, a novel anthelmintic product specifically indicated for the treatment of Sparicotylosis disease caused by the gill monogenean *Sparicotyle chrysophrii* in gilthead sea bream (*Sparus aurata*).

PRODUCT QUALITY

The quality of all Vethellas' veterinary medicinal products is meticulously monitored and consistently verified through regular testing and employing validated methodologies conducted by experienced personnel. The applied manufacturing processes ensure consistency and homogeneity in terms of physical properties of the products. The excipients used are well-established formulations extensively used over decades. The overall properties of the products ensure optimal adhesion and incorporation into the feed, minimizing dust generation and active substance loss. This, in turn, ensures precise dosage delivery, maximizing therapeutic efficacy and ensuring the successful treatment outcome.

MEDICINAL PRODUCTS FOR FARMED FISH

A. ANTIMICROBIAL PRODUCTS

1. OXYTETRACYCLINE 50% VETHELLAS
(Premix for medicated feed)

50% Oxytetracycline Hydrochloride on inactive carrier.

Clinical effectiveness:

- Clinical trials were conducted on 240,000 Atlantic salmon (*Salmo salar*), where *Aeromonas salmonicida* was isolated from the affected fish. The diagnosis was confirmed through bacterial isolation and post-mortem examination. The product was incorporated into the fish feed at a dose of 150 mg per kg body weight per day, providing 75 mg of active oxytetracycline hydrochloride.

It is used for the control of furunculosis/ aeromonosis, vibriosis, and pasteurellosis in **Gilthead sea bream** and **European sea bass.**

OXYTETRACYCLINE 50% VETHELLAS, is used on fish feed at a dose of 150 mg product (equivalent to 75 mg of active Oxytetracycline hydrochloride) per kg body weight per day. It is recommended that the duration of treatment is 5-7 days.

The product may be incorporated into pellets by mixing with the feed mash or can be mixed and adsorbed through surface coating. The inclusion rates in the feed for different feeding rates (depending on the water temperature and the size of the fish) that determine the recommended dosage are indicated on the product's label and SPC.

Withdrawal period:

European Sea bass (*Dicentrarchus labrax*): 560 degree days
Gilthead sea bream: 340 degree days

2. OXYTETRACYCLINE 100% VETHELLAS
(Premix for medicated feed)

100% Oxytetracycline Hydrochloride.

For OXYTETRACYCLINE 100% VETHELLAS, the recommended dose is 75 mg per kg of fish body weight per day.

For the treatment and control of:

- furunculosis caused by *Aeromonas salmonicida* in **Atlantic Salmon**,
- pasteurellosis in **European seabass** caused by *Photobacterium damselae* and
- vibriosis in **European seabass** caused by *Listonella anguillarum* and *Vibrio* species.

A 7–10-day course of treatment is recommended. The product should be incorporated into pellets either mixed in the feed mash or mixed and adsorbed by surface coating.

The inclusion rate in the feed depends on the daily feed intake, which varies according to the size of the fish and the water temperature. The appropriate incorporation rate should be determined according to the instructions provided on the product's label and SPC.

Withdrawal period:

Atlantic salmon: 400 degree days
European Sea bass: 420 degree days

MEDICINAL PRODUCTS FOR FARMED FISH

3. TRIMETHOPRIM-SULPHADIAZINE 50% VETHELLAS
(Premix for medicated feed)

50% Trimethoprim-sulphadiazine on inactive carrier.

Clinical effectiveness:

- Clinical trials were conducted on 500,000 Atlantic salmon, where *Aeromonas salmonicida* was isolated from affected fish. Diagnosis was confirmed through bacterial isolation and post-mortem examination.

- It is indicated for the treatment of bacterial infections in **farmed fish**, particularly for the treatment and control of salmonid furunculosis caused by *Aeromonas salmonicida* and vibriosis due to *Vibrio (Listonella) anguillarum* and other related species.
- Additionally, it has been successfully used in the treatment of columnaris disease and Enteric Red Mouth disease (ERD), caused by *Flexibacter columnaris* and *Yersinia ruckeri,* respectively.

Recommended treatment duration is 7 – 10 days.

The product may be incorporated into feed pellets by mixing with the feed mash or can be mixed and adsorbed through surface coating. The inclusion rates for different feeding rates (depending on the water temperature and the size of the fish) that determine the recommended dosage are indicated on the product's label and SPC.

Withdrawal period:

500 degree days

4. LINACIVET®
(Premix for medicated feed)

50% Oxolinic acid on inactive carrier.

Oxolinic acid is a 1st generation non-fluorinated quinolone, a third-line antimicrobial to be used with caution to treat bacterial pathogens resistant to available first or second line antimicrobials.

Clinical effectiveness:

- Clinical trials were conducted on 16,000 Atlantic salmon, where *Aeromonas salmonicida* was isolated from affected fish. Diagnosis was confirmed through bacterial isolation and post-mortem examination. The product was incorporated into fish feed at a dose of 20 mg per kg body weight per day (equivalent to 10 mg oxolinic acid per kg body weight).

It is indicated for the control and treatment of:

- furunculosis caused by *Aeromonas salmonicida* in both **freshwater** and **seawater salmon** and **farmed rainbow trout** and
- Enteric Red Mouth disease (ERD) in **rainbow trout** caused by *Yersinia ruckeri*.

The recommended dose is 20 mg of the product per kg body weight (equivalent to 10 mg oxolinic acid per kg body weight) daily. It is administered in fish feed, and the recommended treatment duration is 10 days. The product may be pelleted or mixed and adsorbed by surface coating.

Withdrawal period:

100 degree days

MEDICINAL PRODUCTS FOR FARMED FISH

5. SPECLIN®
(Premix for medicated feed)

50% Florfenicol on inactive carrier.

Florfenicol is a synthetic broad-spectrum antibiotic effective against most Gram-positive and Gram-negative bacteria pathogens isolated from domestic animals.

Florfenicol acts by inhibiting protein synthesis at the ribosomal level. Laboratory tests have shown that florfenicol is active against the most commonly isolated bacterial pathogens involved in fish diseases, notably *Aeromonas salmonicida*.

Clinical effectiveness:

- SPECLIN® is a broad-spectrum bactericidal antibiotic that, when administered orally, acts against most Gram-positive and Gram-negative bacteria.

- SPECLIN® is indicated for the treatment of furunculosis in **rainbow trout** (*Oncorhynchus mykiss*) caused by *Aeromonas salmonicida* susceptible to florfenicol, in freshwater fisheries.
- The presence of the disease in the farm should be established before initiating the treatment.

The premix should be incorporated into the feed at the appropriate inclusion rate and medicated feed should be fed at the appropriate feeding rate to the fish in order to deliver a total daily dose rate of 10 mg of florfenicol per kg body weight during 10 consecutive days.

Administration of medicated feed should begin immediately following diagnosis to ensure that fish are able to consume the complete medicated ration.

Withdrawal period: 135 degree days

B. ANTIPARASITIC PRODUCTS

PRAZIVETIN®
(Premix for medicated feed)

50% Praziquantel on inactive carrier.

The active ingredient of PRAZIVETIN®, i.e. praziquantel, is a synthetic broad-spectrum anthelmintic that has been extensively used in veterinary medicine for the treatment of helminthiasis in animals and in human medicine for the treatment of schistosomiasis (caused by digenean trematode blood parasites) for decades. In farmed fish, it has been clinically proven effective against: monogenean worms parasitizing the gills and skin, digenean trematode worms parasitizing the heart cavities and blood vessels, larval stages of digenean trematode worms that are encysted in various organs and intestinal parasitic cestodes (tapeworms).

Clinical effectiveness in gilthead sea bream

Two clinical field trials were conducted in Greece to evaluate the efficacy of PRAZIVETIN® under field conditions in commercial gilthead sea bream farms with cage rearing. In both trials, treatment with PRAZIVETIN® at a dosage of 300 mg/kg body weight per day for 3 consecutive days resulted in a significant reduction in parasite burden. PRAZIVETIN® demonstrated high efficacy against *Sparicotyle chrysophrii* in gilthead sea bream, achieving 86–89% parasite kill (young and mature parasites) following a 3-day treatment.

For administration in fish feed at the rate of 300 mg of product per kg of fish bodyweight daily for 3 consecutive days (equivalent to 150 mg/kg body weight/day praziquantel). The product should be incorporated into extruded feed pellets using surface coating, either by direct mixing of the veterinary medicinal product with fish oil or by spraying the oily mix of the product with fish oil onto the feed pellets.

Withdrawal period: 120 degree days

Important notices for Veterinary Medicinal Products usage:

- **To lower the risk of bacteria becoming resistant,** antimicrobial VMPs should be used in a **Prudent** and **Responsible manner in accordance with** EU's categorization of antibiotics and relevant legal provisions for their use. The company actively supports this approach.
- **Decision to use antiparasitic VMPs should be based on confirmation of the parasitic species and burden to avoid development of resistance by the parasites.**
- **For use of VMPs in other animal species and indications than those indicated in their SPC, consult your veterinarian and ensure compliance with applicable legislation on usage of VMPs by derogation (cascade) provisions (Reg. EU 2019/6, Articles 114, 115).**