SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pyceze 500 mg/mL concentrate for solution for fish treatment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains:

Active substance:
Bronopol 500 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for fish treatment.
A clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Farmed Atlantic salmon and rainbow trout eggs, Atlantic salmon and rainbow trout.

4.2 Indications for use, specifying the target species

The product is indicated for:

- Prevention of growth of fungal infections (*Saprolegnia* spp) in the face of suspected or known challenge in farmed Atlantic salmon eggs and rainbow trout eggs.

- Prevention or reduction of fungal infections (*Saprolegnia* spp) in farmed Atlantic salmon and rainbow trout kept in fresh water.

The product is most effective if used at the first signs of fungal infection.

4.3 Contraindications

Do not use in smolting Atlantic salmon or rainbow trout alevins as studies have indicated increased toxicity at this stage.

4.4 Special warnings for each target species

Treatment with the product is most effective if the infection is treated early and before there is a chance for the fungus to invade the underlying muscle or before there is a build up of a dense mat of dead eggs.

The product must be correctly administered to ensure efficacy (see section 4.9 Amounts to be administered and administration route).

4.5 Special precautions for use

Special precautions for use in animals

Data appears to demonstrate that the product, once diluted in a fixed volume of water, may be degraded by prolonged or repeated exposure to high intensity ultraviolet light. Degradation of the product may alter its toxicity profile. It is therefore recommended that water treated with the product is not passed repeatedly through ultraviolet sterilising filters.
Accurately estimate the volume of water to be treated.
Use at water temperatures of more than 13 °C only in accordance with a benefit/risk assessment by the responsible veterinarian, as efficacy and safety at temperatures above 13 °C has not been demonstrated.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Irritating to eyes, lungs and skin.

Wear protective clothing, impervious gloves, face mask and suitable eye protection when mixing and handling the product. (For instance 0.3 mm nitrile rubber gloves, disposable half mask respirator conforming to European Standard EN149 together with suitable eye protection or a non-disposable respirator conforming to European Standard EN140 with a filter to EN143).

If in contact with the skin, wash immediately and – in case of contact with the eyes – rinse immediately with plenty of water and seek medical advice.

Do not smoke, drink or eat when using the product and wash hands carefully after use.

Other Precautions

This product is designed for use following dilution and waterborne administration. Without any dilution the product is harmful to other aquatic life.

A discharge consent may be required for release of this product into the aquatic environment. This must be obtained, prior to use of the product, from the relevant authority. Otherwise the product should only be used if the flow rate of untreated waters allows for a minimum dilution of the volume of treated water. For fish treatment the product should only be used if the flow rate of untreated water allows a dilution of 1:2000 times the volume of treated water. For egg treatment the product should only be used if the flow rate of untreated water allows a dilution of 1:5000 times the volume of treated water. Where the appropriate dilution of treated water cannot be achieved, the farm must have a discharge process to limit the release of product into the environment to within the parameters described. This can be achieved by the use of holding tanks and ponds, discharge lagoons and biofilters to clean treated water. Where this applies, the user must monitor the discharge concentration to ensure the parameters are not exceeded.

4.6 Adverse reactions (frequency and seriousness)

Occasionally some restlessness has been noted among fish during addition of the product to treatment water.

4.7 Use during pregnancy, lactation or lay

Use in broodstock should only be in accordance with a benefit/risk assessment by the responsible veterinarian because reproductive toxicity has not been established in the target species.

4.8 Interaction with other medicinal products and other forms of interaction

Do not conduct bath treatments with other products at the same time as bath treatments with bronopol.

4.9 Amounts to be administered and administration route

For administration to holding water.

Tear off the internal aluminium seal carefully, and prevent it falling into the bottle.

Eggs:
Treat once daily at 50 mg bronopol/litre (1 mL product /10 litres incubator water) for 30 minutes daily commencing 24 hours after fertilisation and until hatch.
If appropriate to the farm management system, dead eggs should be removed on a regular basis to avoid this becoming a source of further fungal infection.

The correct amount of product per volume of incubator should be measured and mixed with at least 10 litres of water prior to addition to the incubator water. Undiluted product in direct contact may damage the surface of plastic troughs.

Use an appropriate measuring device to measure out the correct amount of product. After use, rinse the measuring device carefully and add the rinsings back into the incubator water. **Flow rates to the incubator must be such that a complete exchange of the incubator water is achieved in 30 minutes or less following the end of the treatment period.**

It is essential that the fish eggs be exposed to a homogeneous concentration of bronopol throughout the treatment period. This can be achieved by ensuring there is continual water movement in the incubator during the treatment period by following the recommendations below for either re-circulation or continuous addition depending on your choice of application. It is important to maintain the flow rate in the incubator during the treatment period at that normally used on the farm to prevent any physical damage to the sensitive eggs.
Use the equations below to calculate the amount of product required, depending on your choice of application. *It is recommended that you do not change the configuration of your system.* The treatment time may appear longer than 30 minutes – this is to allow time for the product to disperse so that each egg receives the correct dose for the correct time.

Re-circulation: (dose = 1 mL per 10 litres water = 50 mg bronopol/litre)

The total treatment dose is added to the system over the time it takes for the water to circulate once through the system (Administration Time) to achieve proper mixing. Circulation of the medicated water is then continued for the treatment time of 30 minutes.

Administration Time (min) = Incubator and pipework volume (litres)

$$\text{Dose of product (mL)} = \frac{\text{Incubator and pipework volume* (litres)}}{\text{Flow rate (litres/min)}} \div 10$$

* = including volume of water the product is diluted in for administration to incubator (Administration Volume)

Add the dose of product during the calculated Administration Time, and then circulate for 30 minutes. The flow of unmedicated water should then resume.

Continuous addition: (dose = 1 mL per 10 litres water = 50 mg bronopol/litre)

Treatment is added to the system over the time it takes for the water already in the system to achieve the correct dose level. Addition of medicated water is then continued for the treatment time of 30 minutes.

$$\text{Administration Time (min)} = \left[\frac{\text{Incubator and pipework volume (litres)}}{\text{Flow rate (litres/min)}} \right] + 30$$

$$\text{Dose of product (mL)} = \left[\frac{\text{Flow rate (litres/min) x Administration Time (mins)}}{10} \right] + \frac{\text{Volume used to dilute the product (Litres)}^*}{10}$$

* = Volume of water product is diluted in for administration to inflow of incubator (Administration Volume)

Add the dose of product during the calculated Administration Time, leaving the in-flow water unchanged.

See package leaflet under further information to illustrate these calculations.

Fish:
Treat once daily at 20 mg bronopol/litre (1 mL product/25 litres water) for 30 minutes daily, for up to 14 consecutive days. Use the equation below to calculate the amount of product required.

$$\text{Dose of product (mL)} = \frac{\text{Treatment Volume (litres)}}{25}$$

After 30 minutes treatment time resume the unmedicated water flow to the treatment unit.

Using an appropriate measuring device add the required volume of product to a bucket containing at least 10 litres of water from the treatment bath. Mix the bucket contents thoroughly and, after stopping the water flow, add to the treatment bath at several positions, spreading the treatment around the treatment bath as much as possible to aid mixing.
After use, rinse the measure and the bucket carefully and add the rinsings back into the treatment bath. Undiluted product in direct contact may damage the surface of plastic tanks.

Flow rates to the treatment unit must be such that a complete exchange of the water is achieved in 60 minutes or less following the end of the treatment period.

It is recommended that oxygen be diffused into the treatment unit throughout the treatment period to maintain an oxygen level above 7 mg/litre and to ensure adequate mixing of the product.

Movement of the fish and oxygen diffusion during treatment will ensure mixing of the product through the treatment water. The treatment unit volume may be reduced to limit the amount of product used. Care should be taken when doing this not to unduly stress the fish by lack of space or oxygen availability.

For treatment of freshwater cages, the net should be raised to a depth of 1 to 2 metres depending on the biomass of the fish. The cage to be treated should then be surrounded by an impervious tarpaulin to completely isolate it. Oxygen should be supplied and treatment carried out as above. Once the 30 minutes treatment time is completed, the tarpaulin should be removed and the nets lowered to the original depth.

Treat daily for up to 14 consecutive days according to veterinary assessment.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Safety studies on both eggs and fish conducted at five times the recommended dose and double the recommended duration (60 minutes) for up to 28 days indicate no adverse effects.

4.11 Withdrawal period(s)

Do not use in salmonid eggs intended for human consumption.
Meat: zero degree days.

5. PHARMACOLOGICAL IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antifungals for dermatological use, other antifungals for topical use.
ATC vet code: QD01AE91

5.1 Pharmacodynamic properties

Mechanism of action:

The mode of action of bronopol was considered to result from blocking thiol containing enzymes such as membrane bound dehydrogenase, causing alterations to the cell membrane, leading to cell leakage and destruction.
The efficacy of bronopol against *Saprolegnia* spp was dose-dependent.
Resistance or a high level of tolerance in micro-organism has not been reported with use of bronopol.

5.2 Pharmacokinetic particulars

Studies conducted in Atlantic salmon with radiolabelled bronopol and residue analysis of rainbow trout treated for 14 days with the product at the recommended dose indicate that bronopol is not absorbed to an appreciable extent when used as a topical treatment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dipropylene glycol monomethyl ether
Purified Water

6.2 Major incompatibilities

Do not conduct bath treatments with other products at the same time as bath treatments with bronopol. Undiluted product in direct contact may damage the surface of plastic tanks.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 6 months
Shelf life after dilution according to directions: used immediately

6.4. Special precautions for storage

Store in the original container.
Keep the container tightly closed.
Do not store above 25 °C.

6.5 Nature and composition of immediate packaging

Polyamide/HDPE bottle (1 litre and 5 litre)

Polypropylene screw cap with an internal low density polyethylene/aluminium/low density polyethylene/paper/polyethylene foam seal (1 litre bottle)

High density polyethylene screw cap with an internal low density polyethylene/polyethylene terephthalate/aluminium/paper/wax/paper/polyethylene foam seal (5 litre bottle)

Polypropylene graduated measuring device (500 mL)

Pack sizes:

Bottle containing 1 Litre

Cardboard box with 1 bottle containing 5 Litres and 1 Polypropylene graduated measuring device (500 mL)
Cardboard box with 4 bottles containing 5 Litres and 4 Polypropylene graduated measuring device (500 mL)

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.
Do not contaminate surface waters or ditches with product or used container.

7. MARKETING AUTHORISATION HOLDER

CZ Vaccines S.A.U.
A Relva s/n – Torneiros
36410 O Porriño
Pontevedra
Spain

8. MARKETING AUTHORISATION NUMBER

Vm 30824/4004

9. DATE OF FIRST AUTHORISATION

03 November 2003

10 DATE OF REVISION OF THE TEXT

November 2023

Approved 11 May 2024