ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AQUI-S vet. 540 mg/mL concentrate for treatment solution for Atlantic salmon and rainbow trout

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: isoeugenol 540 mg/ml

Excipient:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate solution for the treatment of fish. Light yellowish liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Atlantic salmon (*Salmo salar* L.) and rainbow trout (*Oncorhynchus mykiss*).

4.2 Indications for use, specifying the target species

For sedation and anaesthesia of Atlantic salmon and rainbow trout in relation to handling (grading, movement, transport, counting of sea lice, stripping of brood stock fish) and vaccination.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Fish should not be exposed to stress just prior to use of the medicine. Level of dissolved oxygen in the bath for sedation / anaesthesia must be monitored continuously. The recommended minimum oxygen concentration during treatment is 7 mg/L.

4.5 Special precautions for use

Special precautions for use in animals
Level of sedation / anaesthesia must be monitored continuously to avoid overdosing. Safety is not documented < 4 ºC and > 15 ºC. General precaution should be taken for handling of fish at low temperatures as this increases risk of winter ulcers. General precaution should be taken when handling fish at high temperatures as this will increase risk of oxygen failure and disease outbreaks.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In case of accidental ingestion, drink up to two glass of milk or water, seek medical advice immediately and show the package leaflet or the label to the physician. In case of spill on the skin, wash with soap and rinse with water.
Isoeugenol can cause skin irritation and allergic skin reactions. Seek medical advice if allergic skin reaction persists.
People with known hypersensitivity to isoeugenol should avoid contact with the medicine. Personal protective equipment consisting of protective glasses, gloves and suitable clothing must be used when handling the veterinary medicinal product.

Spillage of the veterinary medicinal product on equipment must be rinsed off to minimise risk of accidental contact.
The work area must be well ventilated.

4.6 Adverse reactions (frequency and seriousness)

Overdosing due to high concentration and/or prolonged exposure time may result in depressed respiration and subsequent death.

4.7 Use during pregnancy

Fertility:
Laboratory studies in rats have shown signs of parenteral toxicity, but no observed negative effects (NOAEL) for reproductive parameters at doses < 230 mg/kg/day. NOAEL for developmental toxicity was set to 500 mg/kg/day.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Sedation: 2-5 mg isoeugenol/L depending on desired level of sedation. This corresponds to 3.7 – 9.3 ml Aqui-s/1000 L water. Maximum exposure time 5 hours.

Anaesthesia: 10-14 mg isoeugenol/L depending on desired level of anaesthesia. This corresponds to 18.5 – 25.9 ml Aqui-s/1000 L water. Maximum exposure time: 15 minutes.

Table: Volume of AQUI-S (mL) to be added to the tank dependent on estimated water volume and desired concentration.

Desired concentration (mg isoeugenol/L) / Volume in water tank	***SEDATION***		***ANAESTHESIA***	
	2	**5**	**10**	**14**
100 liter	0.4	0.9	1.9	2.6
1000 liter (1 m^3)	3.7	9.3	18.5	25.9
100 m^3	370	926	-	-

Data indicates that time to desired sedation/anaesthesia is reduced with increasing water temperature.

It is recommended to prepare stock solution by dilution of the veterinary product 1:10 in water. The stock solution should be shaken to ensure a homogenous, milky-white solution. The calculated amount of stock solution is then poured into the anaesthetic bath for sedation/anaesthesia. It is recommended to add the product below water surface to reduce the creation of foam.

The stock solution must be used the same day as prepared. Mixed anaesthetic solution must be changed several times daily.

It is recommended to test the dosing on a smaller group of the representative fish.

When the desired sedation/anaesthesia is reached, the fish must be moved to fresh water for recovery. Do not use Aqui-S if you see signs of deterioration.

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

Overdosing will result in depressed or ceased respiration with increased risk of cardiac arrest and death. In case of overdosing, fish must immediately be moved to fresh water assuring perfusion of the gills until normal respiration is restored.

4.11 Withdrawal period(s)

Meat and offal: 2 degree days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: anaesthetic.
ATCvet code: QN01 AX94.

5.1 Pharmacodynamic properties

Similar to other anaesthetic agents, the exact mode of action is not fully elucidated. It is shown that isoeugenol has neuro-muscular blocking properties in rats. The study indicated blocking of nicotinic receptors in the nervous system. It is likely that a similar mechanism exists in fish. The rapid recovery after exposure indicates a rapid elimination of isoeugenol, and also shows that the mode of action is reversible.

5.2 Pharmacokinetic particulars

Isoeugenol is absorbed over the gills and transported to the nervous system via the blood circulatory system.

Environmental properties

Isoeugenol can be harmful to aquatic organisms.
If concentrated emissions to water occurs the water for the recipient must be sufficiently diluted. Water current must be significant to assure sufficient dilution and spread of large volumes.

Isoeugenol is considered easily biodegradeable in water. Relevant data indicates low or no risk of bioaccumulation in the food chain.

Polysorbate 80 has a slower degradation in water but is considered to have a low risk of bioaccumulation.
Polysorbate 80 is considered to have an acceptable environmental risk if used according to label instructions.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polysorbate 80

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 36 months.
Shelf life after first opening the immediate packaging: 18 months.

Shelf life after dilution according to directions: stock solution of the veterinary product must be used within the same day.

6.4. Special precautions for storage

Protect from frost.
Store in the original container.
Keep the container tightly closed.
Store in a dry place.
Protect from direct sunlight.

6.5 Nature and composition of immediate packaging

HDPE plastic container with HDPE plastic screw cap.
100 ml, 1000 ml and 4000 ml.

100 ml container does contain a drop-dispenser for the ease of dosing small volumes.

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 product should be disposed of in accordance with local requirements.

Undiluted AQUI-S should not be disposed of in waterways as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

~~Scan Aqua AS~~
~~P.O.Box 233~~
~~N-2151 Årnes~~
~~Norway~~
~~Tel: +47 63 60 89 90~~
~~Fax: +47 63 90 89 99~~
~~E-mail: postmaster@scanaqua.com~~

8. MARKETING AUTHORISATION NUMBER(S)

10/8077

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14.05.2013
Date of last renewal: 14.05.2018

10 DATE OF REVISION OF THE TEXT

20.02.2019

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

HDPE plastic container

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AQUI-S vet. 540 mg/mL concentrate for treatment solution for Atlantic salmon and Rainbow trout.

Isoeugenol

2. STATEMENT OF ACTIVE SUBSTANCES

Isoeugenol 540 mg/mL
Emulsifier

3. PHARMACEUTICAL FORM

Concentrate solution for the treatment of fish.

4. PACKAGE SIZE

100 mL, 1000 mL, 4000 mL

5. TARGET SPECIES

Atlantic salmon and Rainbow trout

6. INDICATION(S)

For sedation and anaesthesia of Atlantic salmon and Rainbow trout.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Dosing is identical for Atlantic salmon and Rainbow trout

Sedation: 3.7 – 9.3 mL AQUI-S/1000 litre water depending on targeted level of sedation.
Maximum exposure time: 5 hours.

Anaesthesia: 18.5 – 25.9 mL AQUI-S/1000 litre water depending on targeted level of anaesthesia.
Maximum exposure time: 15 minutes.

8. WITHDRAWAL PERIOD(S)

2 degree days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Protect from frost.
Store in the original container.
Keep the container tightly closed.
Store in a dry place.
Protect from direct sunlight.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

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~~P.O.Box 233~~
~~N-2151 Aarnes~~
~~Norway~~
~~Tel: +47 63 60 89 90~~
~~Fax: +47 63 90 89 99~~
~~E-mail: postmaster@scanaqua.com~~

16. MARKETING AUTHORISATION NUMBER(S)

NO-10/8077

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
AQUI-S vet. 540 mg/mL concentrate for treatment solution for Atlantic salmon and Rainbow trout.

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder: ~~and manufacturer responsible for batch release:~~

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Manufacturer responsible for batch release:
Scan Aqua AS
P.O.Box 233
N-2151 Aarnes
Norway
Tel: +47 63 60 89 90
Fax: +47 63 90 89 99
E-mail: postmaster@scanaqua.com

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

AQUI-S vet. 540 mg/mL concentrate for treatment solution for Atlantic salmon and Rainbow trout

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Isoeugenol 540 mg/mL
Polysorbate 80 (emulsifier)

4. INDICATION(S)

For sedation and anaesthesia of Atlantic salmon and Rainbow trout in relation to handling (grading, movement, transport, counting of sea lice, stripping of brood stock fish) and vaccination.

5. CONTRAINDICATIONS

None

6. ADVERSE REACTIONS

Overdosing will result in depressed or ceased respiration with increased risk of cardiac arrest and death. In case of overdosing, fish must immediately be moved to fresh water assuring perfusion of the gills until normal respiration is restored.

If you notice any side effects, even those not already listed in this package leaflet, or if you think that the medicine has not worked, please inform your veterinary surgeon.

Fertility:
Laboratory studies in rats have shown signs of parenteral toxicity, but no observed negative effects (NOAEL) for reproductive parameters at doses < 230 mg/kg/day. NOAEL for developmental toxicity was set to 500 mg/kg/day.

7. TARGET SPECIES

Atlantic salmon and Rainbow trout.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Sedation: 3.7 – 9.3 mL AQUI-S/1000 litre water depending on targeted level of sedation. This corresponds to 2-5 mg isoeugenol/litre of water. Maximum exposure time 5 hours.

Anaesthesia: 18.5 – 25.9 mL AQUI-S/1000 litre of water depending on targeted level of anaesthesia. This corresponds to 10-14 mg isoeugenol/litre of water. Maximum exposure time: 15 minutes.

Table: Volume of AQUI-S (mL) to be added to the tank dependant on estimated water volume and targeted concentration.

Targeted concentration (mg isoeugenol/L) / Volume in water tank	***SEDATION***		***ANAESTHESIA***	
	2	**5**	**10**	**14**
100 litre	0.4	0.9	1.9	2.6
1000 litre (1 m^3)	3.7	9.3	18.5	25.9
100 m^3	370	926	-	-

Data is indicates that time to targeted sedation / anaesthesia is reduced with increasing water temperature.

9. ADVICE ON CORRECT ADMINISTRATION

Do not use AQUI-S if you notice visible signs of deterioration.

It is recommended to prepare a stock solution of AQUI-S prior to adding it to the anaesthetic bath. This ensures rapid and uniform mixing of AQUI-S in the treatment water. Make a 1:10 stock solution by diluting a measured amount of AQUI-S in 9 equal parts of water. The stock solution should be shaken to ensure a homogenous, milky-white solution. The calculated amount of stock solution is then poured into the anaesthetic bath and it is recommended to add the stock solution beneath the water surface to reduce foaming.
Dosing is temperature dependant. When targeted level of sedation / anaesthesia is reached, the fish must be transferred to fresh water for recovery. Level of sedation / anaesthesia must be monitored continuously to prevent overdosing. It is recommended to test dosing on a small number representative fish.
Level of dissolved oxygen in the bath for sedation / anaesthesia must be monitored continuously. The recommended minimum oxygen concentration during treatment is 7 mg/L.
Safety is not documented < 4 ºC and > 15 ºC. General precaution should be taken when handling of fish at low temperatures as this increases risk of winter ulcers. General precaution should be taken when handling fish at high temperatures as this will increase risk of oxygen failure and disease outbreaks.

Stock solution must be used on the same day as it is prepared. The anaesthetic bath should be replaced several times during the day to maintain efficacy.

The work area must have good ventilation. Personal protective equipment as protective glasses, gloves and suitable clothing must be used when handling the medicine. Spill of medicine on equipment must be rinsed off with water to prevent accidental exposure contact.

10. WITHDRAWAL PERIOD(S)

2 degree days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Protect from frost.
Store in the original container.
Keep the container tightly closed.
Store in a dry place.
Protect from direct sunlight.

Do not use this veterinary medicinal product after the expiry date which is stated on the label.
Shelf life after first opening the container: 18 months
Shelf life after dilution according to directions: use the same day

12. SPECIAL WARNING(S)

Special precautions for use in animals
Level of sedation / anaesthesia must be monitored continuously to avoid overdosing. Safety is not documented < 4 ºC and > 15 ºC. General precaution should be taken for handling of fish at low temperatures as this increases risk of winter ulcers. General precaution should be taken when handling fish at high temperatures as this will increase risk of oxygen failure and disease outbreaks.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In case of accidental ingestion, drink up to two glasses of milk or water, seek medical attention immediately and show the leaflet or the label to the doctor. In case of spill on the skin, wash with soap and rinse with water.
Isoeugenol can cause skin irritation and allergic skin reactions. Seek medical attention if allergic skin reaction persists.
People with known hypersensitivity to isoeugenol should avoid contact with the medicine. Personal protective equipment such as protective glasses, gloves and suitable clothing must be used when handling the medicine.
Spill of the medicine on equipment must be rinsed off to minimise risk of accidental contact.
The work area must have good ventilation.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

04/02/2014

15. OTHER INFORMATION

Not all pack sizes may be marketed.

~~For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.~~

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