Registration file

SLICE

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PART 1

SUMMARY OF THE DOSSIER

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

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1 SUMMARY OF THE DOSSIER

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

1.A SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Slice 2 mg/g premix for medicated feeding stuff.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:
Active substance:

Emamectin benzoate	2.00 mg
(equivalent to 1.76 mg of Emamectin)	

Excipients:

Propylene glycol	25 mg
Butylated hydroxyanisole	0.1 mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff.
A white to off-white free flowing powder.

4. CLINICAL PARTICULARS

4.1 Target species

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

4.2 Indications for use

For the treatment and prevention at group level of infestations of all parasitic stages of sea lice (*Lepeophtheirus* sp. and *Caligus* sp.) on Atlantic salmon (*Salmo salar*) ranging in size from smolts in freshwater (just prior to transfer to seawater) to market weight fish in seawater and rainbow trout (*Oncorhynchus mykiss*).

4.3 Contraindications

Do not use in adult fish intended for broodstock.

Do not use for treatment of smolts in freshwater cages due to potential environmental risks.

4.4 Special warnings

None.

4.5 Special precautions for use

Special precautions for use in animals

Not applicable.

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

Wear gloves, protective work clothing, dust mask and safety glasses with side shields when handling Slice in the preparation of medicated fish feed.

Wash hands thoroughly with soap and water after handling the product or medicated feed before eating or smoking.

Do not smoke or eat while handling the medicated feed.

4.6 Adverse reactions

At the recommended dose emamectin benzoate produced no undesirable effects in the clinical trials, apart from a slight reduction in appetite during the medication period in two trials. A change in the source and pellet size of the medicated diet may have contributed to this effect.

4.7 Use during pregnancy, lactation or lay/pregnancy and lactation

Not applicable.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Administer medicated feed to fish at the recommended feeding rate of 0.5% biomass/day for 7 days which will yield a dose rate of 50 µg/kg biomass/day. If the feeding rate differs from 0.5% biomass/day, then the concentration of Slice in feed must be adjusted proportionately. The following table is provided for reference.

Feeding rate (% biomass of fish)	Concentration of emamectin benzoate in feed medicated with SLICE (mg/kg)	Quantity of SLICE per 1,000 kg of medicated feed (kg)	Quantity of SLICE-medicated feed per 1,000 kg of fish per day (kg)
0.25	**20.0**	**10.0**	**2.5**
0.5	**10.0**	**5.0**	**5.0**
1.0	**5.0**	**2.5**	**10.0**
2.0	**2.5**	**1.25**	**20.0**
3.0	**1.67**	**0.833**	**30.0**
4.0	**1.25**	**0.625**	**40.0**

Slice-medicated fish feed is to be prepared only at commercial fish feed mills and not at fish farms.

Slice is to be coated onto feedstuff of the following type: Extruded cyclindrical pellets of varying thickness and length, e.g., 3.5 mm, 7.0 mm and 10.0 mm.

Recommended Method of Incorporation:

Slice may be coated onto the surface of non-medicated fish feed in the following manner:

a. Standard feed is transported by a conveyor belt to a fractioning sieve where dust and fragments are sorted out.

b. The sorted pellets are transferred to an intensive mixer.

c. The pellets are dry-mixed/coated with a pre-determined amount of Slice for up to 2 minutes

d. 0.5% to 1% fish or vegetable oil is added and mixing continued for up to 5 minutes. The added oil seals the premix powder to the feed pellet.

e. At the completion of mixing, the product is transferred to a feeder tank for packaging into sacks.

The recommended maximum number of marine treatments is 5 per 2 year growth cycle and not more than 3 per 12 month period.

Smolts should only be treated when raised either in tanks or in flowing water waterways (see contraindications).

Smolts should transfer to seawater 1-2 days after the seven day treatment period has ended.

To reduce the possibility of resistance development in sea lice it is recommended that emamectin benzoate is used in integrated control programs with the following considerations:

- Administration of the correct dosage rate over the full seven day period
- Medication of an appropriate amount of feed to ensure complete and homogeneous consumption
- Careful feeding practices to monitor feeding behavior
- Use of the product in the absence of any incurrent disease affecting appetite
- Simultaneous medication of all fish on a site
- Coordination of treatments of all farms in a loch or bay system to reduce cross-infestation
- Use of good management practices such as single age sites, all-in-all-out systems and fallowing between production cycles
- Use in rotation with other authorized therapeutic agents and/or in collaboration with other natural agents such as cleaner fish

It is important that the level of infestation and the effectiveness of control measures are monitored by routine counting of sea lice stages on samples of representative fish. Counts should be conducted on at least five fish from each of 20% of cages on the farm at weekly intervals in summer and every second week in winter. Treatment should only be initiated when the number of sea lice per fish reaches a level so that effective sea lice population control can be established.

4.10 Overdose

Emamectin benzoate administered to Atlantic salmon smolts in freshwater at 5.4 times the recommended dose produced dark skin colouration and incoordination during the treatment period.

Emamectin benzoate administered to Atlantic salmon in seawater at seven times the recommended dose produced lethargy, dark skin colouration and incoordination commencing on the fifth day of medication and inappetance commencing two days after treatment.

Emamectin benzoate administered to rainbow trout at eight times the recommended dose produced lethargy, dark skin colouration and inappetance.

Recovery was not evident in the week following treatment, in either fish treated in freshwater or in seawater. There is no known antidote.

4.11 Withdrawal periods

Atlantic salmon (*Salmo salar*)	Zero days
Rainbow trout (*Oncorhynchus mykiss*)	336 degree days

To ensure that tissue residues do not exceed the MRL, fish must not be treated more than once in the 60 days prior to the first fish being harvested for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Avermectin class of endectocides

ATCvet code: QP54AA06

5.1 Pharmacodynamic properties

Emamectin benzoate is a semi-synthetic avermectin. Avermectins are macrocyclic compounds produced by the soil microorganism *Streptomyces avermitilis* and are characterised by a 16-membered lactone ring with an attached dioleandrosyl group.

The precise mechanism by which emamectin benzoate kills the various sea lice species has not been elucidated. However, extensive research on the mode of action of avermectin compounds against invertebrate species has shown that the avermectins competitively bind to glutamate-gated chloride channels on invertebrate nerves. The distribution of glutamate-gated chloride channels in the invertebrate may be localised to specific muscles such as those of the pharyngeal pump.

5.2 Pharmacokinetic particulars

Emamectin benzoate is relatively slowly absorbed but it is also widely distributed to the tissues. Excretion is also relatively slow.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol

Butylated hydroxyanisole

Maize starch

Maltodextrin M-100

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 24 months.

Shelf life after incorporation into meal or pelleted feed: 3 months

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and composition of immediate packaging

Container: Laminate Foil Pouch (12" x 15") composed of polypropylene/low density polyethylene/aluminium foil. Fill weight 2.5 kg/pouch.

Closure: Pouch is heat sealed on three sides

Package Size: 2.5 kg pouch

Fibre Drum containing 8 x 2.5 kg pouches

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

Any unused product or waste materials should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

Intervet International B.V.

Wim de Körverstraat 35

5831 AN Boxmeer

The Netherlands

1.B PROPOSAL FOR LABELLING AND PACKAGE LEAFLET

PARTICULARS TO APPEAR ON THE OUTER PACKAGE (BOX) DRUM/POUCH

NAME OF THE VETERINARY MEDICINAL PRODUCT

Slice 2 mg/g premix for medicated feeding stuff.

STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each 2.5 kg pouch of Slice contains 5 g of emamectin benzoate (equivalent to 2 mg/g) and 0.25 g butylated hydroxyanisole (equivalent to 0.1 mg/g) as a preservative.

PHARMACEUTICAL FORM

Premix for medicated feeding stuff.

A white to off-white free flowing powder.

PACKAGE SIZE

2.5 kg pouch

8 x 2.5 kg

INDICATIONS

For the treatment and prevention at group level of infestations of all parasitic stages of sea lice (*Lepeophtheirus* sp. and *Caligus* sp.) on Atlantic salmon (*Salmo salar*) ranging in size from smolts in freshwater (just prior to transfer to seawater) to market weight fish in seawater and rainbow trout (*Oncorhynchus mykiss*).

METHODS AND ROUTES OF ADMINISTRATION

Administer medicated feed to fish at the recommended feeding rate of 0.5% biomass/day for 7 days which will yield a dose rate of 50 µg/kg biomass/day. If the feeding rate differs from 0.5%

biomass/day, then the concentration of Slice in feed must be adjusted proportionately. The following table is provided for reference.

Feeding rate (% biomass of fish)	Concentration of emamectin benzoate in feed medicated with SLICE (mg/kg)	Quantity of SLICE per 1,000 kg of medicated feed (kg)	Quantity of SLICE-medicated feed per 1,000 kg of fish per day (kg)
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Recommended Method of Incorporation:

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a. Standard feed is transported by a conveyor belt to a fractioning sieve where dust and fragments are sorted out.

b. The sorted pellets are transferred to an intensive mixer.

c. The pellets are dry-mixed/coated with a pre-determined amount of SLICE for up to 2 minutes.

d. 0.5% to 1% fish or vegetable oil is added and mixing continued for up to 5 minutes. The added oil seals the premix powder to the feed pellet.

e. At the completion of mixing, the product is transferred to a feeder tank for packaging into sacks.

The recommended maximum number of marine treatments is 5 per 2 year growth cycle and not more than 3 per 12 month period.

Smolts should only be treated when raised either in tanks or in flowing waterways (see contra-indications).

Smolts should be transferred to seawater 1 - 2 days after the seven day treatment period has ended.

To reduce the possibility of resistance development in sea lice it is recommended that emamectin benzoate is used in integrated control programs with the following considerations:

- Administration of the correct dosage rate over the full seven day period
- Medication of an appropriate amount of feed to ensure complete and homogeneous consumption
- Careful feeding practices to monitor feeding behavior

- Use of the product in the absence of any intercurrent disease affecting appetite
- Simultaneous medication of all fish on a site
- Coordination of treatments of all farms in a loch or bay system to reduce cross-infestation
- Use of good management practices such as single age sites, all-in-all-out systems and fallowing between production cycles
- Use in rotation with other authorized therapeutic agents and/or in collaboration with other natural agents such as cleaner fish.

It is important that the level of infestation and the effectiveness of control measures are monitored by routine counting of sea lice stages on samples of representative fish. Counts should be conducted on at least five fish from each of 20% of cages on the farm at weekly intervals in summer and every second week in winter. Treatment should only be initiated when the number of sea lice per fish reaches a level so that effective sea lice population control can be established.

WITHDRAWAL PERIODS

Atlantic salmon	Zero days
Rainbow trout	336 degree days

To ensure that tissue residues do not exceed the MRL, fish must not be treated more than once in the 60 days prior to the first fish being harvested for human consumption.

SPECIAL WARNINGS

Do not use in adult fish intended for broodstock.

Do not use for treatment of smolts in freshwater cages due to potential environmental risks.

Wear gloves, protective work clothing, dust mask and safety glasses with side shields when handling SLICE in the preparation of medicated fish feed.

Wash hands thoroughly with soap and water after handling the product or medicated feed and before eating or smoking.

Do not smoke or eat while handling the medicated feed.

At the recommended dose emamectin benzoate produced no undesirable effects in the clinical trials, apart from a slight reduction in appetite during the medication period in two trials. A change in the source and pellet size of the medicated diet may have contributed to this effect.

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Emamectin benzoate administered to rainbow trout at eight times the recommended dose produced lethargy, dark skin colouration and inappetance.

Recovery was not evident in the week following treatment, in either fish treated in freshwater or in seawater. There is no known antidote.

SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.

SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS

Any unused product or waste materials should be disposed of in accordance with local requirements.

FOR ANIMAL TREATMENT ONLY

For animal treatment only

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

READ THE PACKAGE LEAFLET BEFORE USE

Read the package leaflet before use.

MARKETING AUTHORISATION HOLDER

Product of Intervet International B.V., Boxmeer, The Netherlands

BATCH NUMBER

Batch

EXPIRY DATE

EXP: