ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon concentrate for solution for injection of female salmonid fish

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

VIAL CONTAINING CONCENTRATE:

Active substance(s)

Azagly-nafarelin 1600 μg/ml as azagly-nafarelin acetate.

Excipients

Benzyl alcohol (1%)

VIAL CONTAINING SOLVENT:

Excipients

Benzyl alcohol (1%)

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for injection

4. CLINICAL PARTICULARS

4.1 Target species

Female salmonid fish such as Atlantic salmon (*Salmo salar*), rainbow trout (*Oncorhynchus mykiss*), brown trout (*Salmo trutta*) and Arctic charr (*Salvelinus alpinus*).

4.2 Indications for use, specifying the target species

Induction and synchronisation of ovulation for the production of eyed-eggs and fry.

4.3 Contraindications

Do not use Gonazon before approximately 10% of the specific broodstock population has ovulated naturally.

The product should not be used in fish maintained in water temperatures that would normally inhibit ovulation as this can result in a decrease in egg quality.

4.4 Special warnings for each target species

Reductions in fecundity, egg quality and survival to the eyed-egg stage have been observed in fish treated with azagly-nafarelin. In some cases this can be related to the use of the compound too early in the spawning season.

It is recommended to strip fish after injection at intervals of approximately 50-100 degree days.

For Arctic charr, injections should be given only if the water temperature is < 8°C.

The long term effects of azagly-nafarelin on treated broodstock fish have not been studied.

4.5 Special precautions for use

Special precautions for use in animals

High standards of biosecurity must be observed at the time of injection in order to prevent introduction and spread of infectious diseases between broodstock fish.

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

Operators should wear gloves when mixing the concentrate solution with the solvent.

Avoid self injection.

In case of accidental contact with either the skin or the eyes, rinse thoroughly with water. Medical advice should be sought immediately in cases in which the concentrated solution or several ml of the diluted solution are spilled onto the skin or into the eyes or in the case of accidental self-injection. The package insert or the label should be shown to the physician.

Operators should wash their hands after use of the product.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Not applicable.

4.8 Interaction with other medicinal products and other forms of interaction

No information on interactions with other veterinary medicinal products is available.

4.9 Amounts to be administered and administration route

Fish should be anaesthetised.
Inject intraperitoneally along the central line, 1/2 to 1 fin length in front of the pelvic fin base.

The recommended dose is 32 µg/kg body weight.
This dose should be administered in the preferred volume for the particular body weight of fish. The supplied solvent is used to dilute the concentrate to the correct dilution to allow for optimisation of injection volumes for fish of widely varying body weights.

The empty, sterile vial is intended to be used for mixing the concentrate and solvent. Additional sterile vials will be supplied on request.

The table below provides the required volume of concentrate and the required volume of solvent to obtain the preferred injection volume of 0.1 ml/ kg fish, 0.2 ml/kg fish, 0.5 ml/kg fish or 1 ml/kg fish.

		Preferred injection volume per kg fish (depending on fish size)*			
		0.1 ml	**0.2 ml**	**0.5 ml**	**1.0 ml**
Total kg of fish to be injected	**Concentrate volume**	**Solvent volume**			
50 kg	1 ml	4 ml	9 ml	24 ml	49 ml
100 kg	2 ml	8 ml	18 ml	48 ml	98 ml

* this volume will be minimized for the species with the largest body weights.

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

An overdose will not accelerate the onset or increase the degree of ovulation. A reduction in the egg quality is seen after administration of doses above the recommended therapeutic dose. No antidotes are available.

4.11 Withdrawal period(s)

Zero days.

5. PHARMACOLOGICAL PROPERTIES

Pharmaceutical group: gonadotrophin-releasing hormone.
ATC vet code: QH01CA

5.1 Pharmacodynamic properties

Azagly-nafarelin is a synthetic analogue of gonadotrophin-releasing hormone (GnRH). GnRH is synthesised by neurones in the hypothalamus in all vertebrate species. It controls reproduction in fish by modulating the secretion of the pituitary gonadotrophins, luteinizing hormone (LH) and follicle stimulating hormone (FSH), also known in fish endocrinology as GtH-II and GtH-I, respectively. GnRH analogues are peptides.

Azagly-nafarelin, like other GnRH analogues, mimics the action of GnRH, through modulation of the secretion of LH and FSH in mammals and fish.

5.2 Pharmacokinetic particulars

Azagly-nafarelin is rapidly absorbed after intraperitoneal treatment in rainbow trout. The distribution and metabolism of azagly-nafarelin have not been studied in the target species. Azagly-nafarelin is rapidly eliminated from plasma after IP treatment in rainbow trout. The elimination half-life ($T_{1/2}$) and Mean Residence Time of azagly-nafarelin in trout after IP treatment of 32 µg/kg BW are 4.9 h and 6.8 h, respectively.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Sodium acetate (tri-hydrate)
Acetic acid, glacial
Sodium chloride / Hydrochloric acid 4N (for pH adjustment)

Water for injection

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 sage: 3 years.
Shelf life after first opening the immediate packaging: 28 days.
Shelf life after dilution according to directions: the product should be used immediately.

6.4 Special precautions for storage

Store and transport at 2°C - 8°C (in a refrigerator).
Do not freeze.

6.5 Nature and composition of immediate packaging

Carton**:** 1 concentrate vial and 1 solvent vial.

Concentrate vial: 3 ml brown glass vial containing 2 ml of solution; rubber stopper and crimp cap.

Solvent vial: 100 ml clear glass vial containing 100 ml of solution; rubber stopper and crimp cap.

Sterile container: 50-ml empty

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.

7. MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/03/040/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22.07.2003 / 13.06.2008

10. DATE OF REVISION OF THE TEXT

13.06.2008

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon 18.5 mg implant for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Azagly-nafarelin 18.5 mg per implant

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Implant

Gonazon implant is a solid, off white, 14x3x1 mm implant.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs (bitches)

4.2 Indications for use, specifying the target species

Prevention of gonadal function in bitches *via* long term blockade of gonadotrophin synthesis.

4.3 Contraindications

Do not use in bitches (prepubertal and adult) intended for breeding (see section 4.7).

4.4 Special warnings

Based on field trial data, it is evident that the implant may not be retained in a proportion (1.2%) of treated bitches. If the implant cannot be palpated in the month following administration, the owner is encouraged to seek veterinary advice as efficacy cannot be ensured in these cases.

At the end of a one year treatment, it may not be possible to locate and remove the implant in approximately 10% of cases. To minimise this problem, caution needs to be exercised to ensure that the implant is administered by subcutaneous injection, particularly in dogs with pronounced depots of subcutaneous fat. Inability to locate and remove Gonazon will not have serious effects on the general health of the dog. However, the timing of return to heat cannot be predicted.

Following a single administration, return to ovarian activity after implant removal may take longer in bitches treated before puberty (average 255 days, range 36-429 days) than in adult bitches (average 68 days, range 12 to 264 days). A large proportion (68%) of the first heat after a single treatment in adult bitches were non-ovulatory. In addition following a repeat treatment, the timing of a return to heat cannot be accurately predicted. No data are available on repeat treatments in prepubertal bitches.

Accidental ingestion of the implant by the dog will not affect its health, since the oral bio-availability of GnRH agonists is very low.

4.5 Special precautions for use

Special precautions for use in animals

Treatment in proestrus will not suppress that particular heat (proestrus and oestrus).

In the absence of clinical information, do not treat bitches less than 3 kg bodyweight and bitches of giant breeds over 45 kg bodyweight.

In adult bitches, heat is commonly induced in the first month following the first administration of the implant. The frequency of induced heat is lower when the first treatment is administered in metoestrus (32%) than in anoestrus (84%). Therefore, the first treatment should preferably be administered in metoestrus. The incidence of induced heat following administration of a repeat treatment to bitches that have not shown signs of oestrus following a previous administration of the product is low (estimated to be 8%).

The risk of inducing a fertile heat is low in metoestrus (5%). Administration of Gonazon at other stages of the cycle may induce heat that may be fertile. If a bitch becomes pregnant following induced heat, embryonic resorption or abortion may occur. Therefore, if heat is observed, contact with male dogs should be prevented until all signs of heat (vulvar swelling, bleeding and attractiveness to male dogs) cease.

Induced heat is not observed if treatment is started before puberty. In addition, the frequency of induced heat is lower in younger bitches than in older bitches.

A proportion of bitches that show induced heat may subsequently develop pseudopregnancy. However, based on field trial data, the incidence of pseudopregnancy in treated bitches is not greater than in control (untreated) bitches.

The product when administered at the recommended treatment dose is ineffective in bitches aged 7 years or older.

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

Personal protective equipment, consisting of gloves, should be worn when handling the veterinary medicinal product.

Avoid accidental self-injection. In case of accidental self-administration of the implant, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Owing to their pharmacological activity (inhibition of the production of sex steroids), administration of GnRH agonists to bitches might be associated with vaginitis.

4.7 Use during pregnancy, lactation or lay

The use is not recommended during pregnancy and lactation. Laboratory studies have shown that administration of the product during early pregnancy in the bitch is unlikely to affect that pregnancy (that is, pregnancy will be carried to full term with the birth of viable pups).

The product is contraindicated in bitches intended for breeding (adult and prepubertal) as laboratory studies in which dogs received 3 simultaneous implants for a period of 12 months revealed a reduction in the numbers of live pups at whelping and weaning compared to an untreated control group.

4.8 Interaction with other medicinal products and other forms of interaction

Azagly-nafarelin is a peptide that is primarily degraded by peptidases and not by cytochrome P-450 enzymes. Therefore, drug interactions would not be expected to occur. In a limited laboratory study, co-administration of Gonazon and short-acting progestagens has been shown to be well tolerated. However, interactions with other medicinal products have not been investigated.

4.9 Amounts to be administered and administration route

The recommended dose is one implant per bitch.
The implant may be administered to bitches from the age of four months.
In adult bitches, the first treatment should be administered preferably in metoestrus.
The duration of prevention of gonadal function is obtained as detailed in the table below:

	Age at which treatment is started	
	4 months – 3 years old	3 - 6 years old
Average duration of blockade (standard deviation)	12 months (± 24 days)	11 months (± 93 days)

Based on field data, the occurrence of oestrus after a single treatment was prevented for 12 months or more in 75% of treated adult bitches and ≥ 90 % of treated prepubertal bitches. However, it should be noted that within the first month after treatment a proportion of treated bitches also experienced an induced heat (see section 4.5). The product, when administered at the recommended treatment dose, is ineffective in bitches aged seven years or older.

In bitches where gonadal function has been successsfully prevented for a period of 12 months, then a second treatment may be administered at that time for continued prevention of oestrus. There are no data available for animals treated on more than two occasions.

ADMINISTRATION:

Gonazon should be injected subcutaneously, in the ventral anterior abdominal wall, in the region of the umbilicus, using aseptic technique. The method of administration is as follows:

1. Position the bitch on her back. Prepare a small area (*e.g.* 4 cm²) of the ventral anterior abdominal/umbilical region for an aseptic procedure.
2. Open the foil pouch using the pre-cut incision to remove the sterile injection device.
3. Remove the needle cap. Unlike liquid injections, there is no need to remove air bubbles as attempts to do so may displace the implant from the needle.
4. Using aseptic technique, raise a small piece of skin in the region of the dogs umbilicus. With the bevel of the needle facing upwards, insert the needle at a 30 degree angle to the tented skin in a single motion, subcutaneously.
5. Take care to avoid penetrating the abdominal wall musculature or fat tissue.
6. With your free hand, use the thumb grip to hold the injection device in position, and depress the plunger as far as it can go. This retracts the needle and withdraws it, leaving the implant beneath the skin. Withdraw the needle from the skin.
7. Ensure that the administration site is clean and dry. Instruct the owner to keep the administration site clean and dry for 24 hours.
8. Record the date of treatment in the clinical records of the animals.

REMOVAL:

Chemical restraint (sedation and/or general anaesthesia) may be required for implant removal.
Position the dog as described for administration of the implant.

1. Locate the implant by gentle digital palpation of the administration site. Prepare the site for an aseptic technique.
2. After adequate (local) anaesthesia is present, apply gentle digital pressure to the far end of the implant. Make a stab incision, approximately 5 mm long, along the elevated near end of the implant. Push the implant gently towards the stab incision. If necessary, dissect away any fibrous tissue to free the implant. Grasp it with forceps and remove.
3. Instruct the owner to keep the administration site clean and dry for 24 hours.

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

Risk of overdose is negligible owing to the type of formulation and administration (single dose implant for subcutaneous administration). Simultaneous administration of five implants during a one-year period was well tolerated.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gonadotrophin-Releasing Hormone (GnRH)
ATCvet code: QH01CA

Azagly-nafarelin, a GnRH agonist, has biphasic effects on the pituitary gland when administered continuously. Initially, it stimulates pituitary function and secretion of the gonadotrophins LH (luteinising hormone) and FSH (follicle stimulating hormone). This brief phase may result in induced heat within one to four weeks following the first administration of the implant (see section 4.5). Long-term administration results in pituitary desensitisation to the effects of GnRH resulting in a suppression of LH and FSH secretion by the pituitary. As a consequence, there is no follicular follicle growth (hence no oestrus is observed) and no ovulation. The transition between the stimulatory and inhibitory effects is completed within approximately one month.

5.2 Pharmacokinetic particulars

Absorption: Following subcutaneous administration of a single implant to dogs (approximate weight of 10 kg), maximum serum concentrations (0.13 µg/ml) of azagly-nafarelin are reached around 3.5 hours. These maximal azagly-nafarelin concentrations are followed by a slow decline in circulating azagly-nafarelin concentrations lasting up to 12 months.
Distribution: The apparent volume of distribution of azagly-nafarelin following intravenous bolus administration, at a dose equivalent to the content of one implant, is 0.12 l/kg.
Metabolism and excretion: The clearance of azagly-nafarelin following intravenous administration of the same dose is 0.46 l/h and the elimination half-life is 1.8 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cured elastomer, resulting from the polymerisation of polydimethylsiloxane and tetrapropylorthosilicate in the presence of stannous octoate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and composition of immediate packaging

Single disposable injection device, preloaded inside a hypodermic needle covered with a protective cap. The unit is sterile and comes in a sealed, light-proof, aluminium foil laminate pouch, packed in an individual carton box.

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.

7. MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/03/040/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22.07.2003 / 13.06.2008

10. DATE OF REVISION OF THE TEXT

13.06.2008

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu/.

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO SAFE AND EFFECTIVE USE

D. STATEMENT OF THE MRLs

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Gonazon for fish:
Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Gonazon for dogs:
Intervet GesmbH
Siemensstrasse 107
A-1210 Wien
Austria

B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

Veterinary medicinal product subject to prescription.

The holder of this marketing authorisation must inform the European Commission about the marketing plans for the medicinal product authorised by this decision.

C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE PRODUCT

Not applicable.

D. STATEMENT OF THE MRLs

Substance	MRL status	Comments
Azagly-nafarelin	Annex II for Salmonidae[1]	Not for use in fish from which eggs are produced for human consumption
Sodium acetate (tri-hydrate)	Annex II for all food producing species	Approved food additive (E 262), CR No 2034/96
Acetic acid (glacial)	Annex II for all food producing species	Approved food additive (E 260), CR No 2034/96
Benzyl alcohol	Annex II for all food producing species. For use as excipient	CR No 1442/95
Sodium chloride	Annex II for all food producing species	CR No 2796/95
Sodium hydroxide	Included in Annex II for all food producing species	Approved food additive (E 524), CR No 2034/96
Hydrochloric acid	Annex II for all food producing species, for use as excipient.	CR No 1442/95
Water for injections	Not within the scope of Council Regulation 2377/90	

[1] Regulation 1530/02 / OJL230 of 28 August 2002

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon concentrate for solution for injection of female salmonid fish

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

- **VIAL CONTAINING CONCENTRATE:**

Active substance(s)

Azagly-nafarelin 1600 µg/ml as azagly-nafarelin acetate.

Excipients

Benzyl alcohol

- **VIAL CONTAINING SOLVENT:**

Excipients

Benzyl alcohol

3. PHARMACEUTICAL FORM

Concentrate for solution for injection.

4. PACKAGE SIZE

Carton containing one vial with 2 ml of concentrate solution and 1 bottle with 100 ml of solvent. An empty sterile mixing vial is supplied separately. Additional sterile vials will be supplied on request.

5. TARGET SPECIES

Female salmonid fish such as Atlantic salmon (*Salmo salar*), rainbow trout (*Oncorhynchus mykiss*), brown trout (*Salmo trutta*) and Arctic charr (*Salvelinus alpinus*).

6. INDICATION(S)

Induction and synchronisation of ovulation for the production of eyed-eggs and fry.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Zero days.

9. SPECIAL WARNING(S), IF NECESSARY

Reductions in fecundity, egg quality and survival to the eyed-egg stage have been observed in fish treated with azagly-nafarelin too early in the spawning season. It is recommended to strip fish after injection at intervals of approximately 50-100 degree days. For Arctic charr, injections should be given only if the water temperature is < 8°C.

High standards of biosecurity must be observed at the time of injection in order to prevent introduction and spread of infectious diseases between broodstock fish.

The long term effects of azagly-nafarelin on treated broodstock fish have not been studied.

Operators should wear gloves when mixing the concentrate solution with the solvent. Read the package insert before use.

10. EXPIRY DATE

"Month/Year"
After dilution, the product should be used immediately.

11. SPECIAL STORAGE CONDITIONS

Store and transport at 2°C - 8°C (in a refrigerator).
Do not freeze.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of 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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/03/040/001

17. MANUFACTURER'S BATCH NUMBER

<Batch> <Lot> <BN> {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton Box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon 18.5 mg implant for dogs

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Azagly-nafarelin (18.5 mg)

3. PHARMACEUTICAL FORM

Implant

4. PACKAGE SIZE

One implant.

5. TARGET SPECIES

Dog (bitches)

6. INDICATION(S)

Prevention of gonadal function in bitches *via* long term blockade of gonadotrophin synthesis.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous administration.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of 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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/03/040/002

17. MANUFACTURER'S BATCH NUMBER

<Batch> <Lot> <BN> {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

2 ml concentrate vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon concentrate for solution for injection of female salmonid fish

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Azagly-nafarelin 1600 μg/ml as azagly-nafarelin acetate.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

2 ml

4. ROUTE(S) OF ADMINISTRATION

Intraperitoneal (IP) use

5. WITHDRAWAL PERIOD

Zero days

6. BATCH NUMBER

<Batch> <Lot> {number}

7. EXPIRY DATE

EXP {month/year}
After dilution, the product should be used immediately.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only- to be supplied only on veterinary prescription.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Sachet

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon 18.5 mg implant for dogs

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Azagly-nafarelin

3. CONTENTS BY WEIGHT, BY VOLUME OR NUMBER OF DOSES

One implant.

4. ROUTE(S) OF ADMINISTRATION

Subcutaneous administration.

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Batch < number >

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vial containing solvent

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon concentrate for solution for injection of female salmonid fish

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Excipients

Benzyl alcohol

3. PHARMACEUTICAL FORM

Solvent for solution for injection.

4. PACKAGE SIZE

Carton containing one vial with 2 ml of concentrate solution and 1 bottle with 100 ml of solvent. An empty sterile mixing vial is supplied separately. Additional sterile vials will be supplied on request.

5. TARGET SPECIES

Female salmonid fish such as Atlantic salmon (*Salmo salar*), rainbow trout (*Oncorhynchus mykiss*), brown trout (*Salmo trutta*) and Arctic charr (*Salvelinus alpinus*).

6. INDICATION(S)

Induction and synchronisation of ovulation for the production of eyed-eggs and fry.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Zero days.

9. SPECIAL WARNING(S), IF NECESSARY

Reductions in fecundity, egg quality and survival to the eyed-egg stage have been observed in fish treated with azagly-nafarelin too early in the spawning season. It is recommended to strip fish after injection at intervals of approximately 50-100 degree days. For Arctic charr, injections should be given only if the water temperature is < 8°C.

High standards of biosecurity must be observed at the time of injection in order to prevent introduction and spread of infectious diseases between broodstock fish.

The long term effects of azagly-nafarelin on treated broodstock fish have not been studied.

Operators should wear gloves when mixing the concentrate solution with the solvent. Read the package insert before use.

10. EXPIRY DATE

"Month/Year"
After dilution, the product should be used immediately.

11. SPECIAL STORAGE CONDITIONS

Store and transport at 2°C - 8°C (in a refrigerator).
Do not freeze.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of 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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/03/040/001

17. MANUFACTURER'S BATCH NUMBER

<Batch> <Lot> <BN> {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Separate empty sterile containers

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Azagly-nafarelin 1600 µg/ml as azagly-nafarelin acetate.

3. CONTENTS BY WEIGHT, BY VOLUME OR NUMBER OF DOSES

50 ml

4. ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

5. WITHDRAWAL PERIOD

Zero days.

6. BATCH NUMBER

<Batch> <Lot> {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Gonazon concentrate for solution for injection of female salmonid fish

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

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon concentrate for solution for injection of female salmonid fish

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

Azagly-nafarelin 1600 µg/ml as azagly-nafarelin acetate.

Excipient: Benzyl alcohol

4. INDICATION(S)

Induction and synchronisation of ovulation for the production of eyed-eggs and fry.

5. CONTRAINDICATIONS

Do not use Gonazon before approximately 10% of the specific broodstock population has ovulated naturally.

The product should not be used in fish maintained in water temperatures that would normally inhibit ovulation as this can result in a decrease in egg quality.

6. ADVERSE REACTIONS

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Female salmonid fish such as Atlantic salmon (*Salmo salar*), rainbow trout (*Oncorhynchus mykiss*), brown trout (*Salmo trutta*) and Arctic charr (*Salvelinus alpinus*).

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

9. ADVICE ON CORRECT ADMINISTRATION

Inject intraperitoneally along the central line, 1/2 to 1 fin length in front of the pelvic fin base. Fish should be anaesthetised.

The dose should be administered in the preferred volume for the particular body weight of fish. The supplied solvent is used to dilute the concentrate to the correct dilution to allow for optimisation of the preferred injection volumes for fish of widely varying body weights.

The empty, sterile vial is intended to be used for mixing the concentrate and solvent. Additional sterile vials will be supplied on request.

The table below provides the required volume of concentrate and the required volume of solvent to obtain thepreferred injection volumes of 0.1 ml/kg fish, 0.2 ml/kg fish, 0.5 ml/kg fish or 1 ml/kg fish.

		Preferred injection volume per kg fish (depending on fish size) *			
		0.1 ml	**0.2 ml**	**0.5 ml**	**1.0 ml**
Total kg of fish to be injected	**Concentrate volume**	**Solvent volume**			
50 kg	1 ml	4 ml	9 ml	24 ml	49 ml
100 kg	2 ml	8 ml	18 ml	48 ml	98 ml

* this volume will be minimized for the species with the largest body weight

The diluted solution for injection should be used immediately.

10. WITHDRAWAL PERIOD

Zero days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Store at 2 – 8°C (in a refrigerator).
Do not freeze.
Do not use after the expiry date stated on the label.
After first opening the container, the solvent may be stored for 28 days.
After dilution, the product should be used immediately.

12. SPECIAL WARNING(S)

Do not mix with other medicinal products.
Operators should wear gloves when mixing the concentrate solution with the solvent.

Avoid self injection.

In case of accidental contact with either the skin or the eyes, rinse thoroughly with water. Medical advice should be sought immediately in cases in which the concentrated solution or several ml of the

diluted solution are spilled onto the skin or into the eyes or in the case of accidental self-injection. The package insert or the label should be shown to the physician

Operators should wash their hands after use of the product.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

13.06.2008

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu

15. OTHER INFORMATION

None.

PACKAGE LEAFLET
Gonazon 18.5 mg implant for dogs

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

Marketing authorisation holder:
Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Manufacturer responsible for the batch release:
Intervet GesmbH
Siemensstraβe 107
A-1210 Wien
Austria

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonazon 18.5 mg implant for dogs

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

Azagly-nafarelin 18.5 mg

4. INDICATION(S)

Prevention of gonadal function in bitches *via* long term blockade of gonadotrophin synthesis.

5. CONTRAINDICATIONS

Do not use in bitches (prepubertal and adult) intended for breeding.

6. ADVERSE REACTIONS

Owing to their pharmacological activity (inhibition of the production of sex steroids), administration of GnRH agonists to bitches might be associated with vaginitis.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dog (bitches).

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

For subcutaneous administration.
In the absence of clinical information, do not treat bitches less than 3 kg bodyweight and bitches of giant breeds over 45 kg bodyweight.
The recommended dose is one implant per bitch.
The implant may be administered to bitches from the age of four months.
In adult bitches, the first treatment should be administered preferably in metoestrus.
The duration of prevention of gonadal function is obtained as detailed in the table below:

	Age at which treatment is started	
	4 months – 3 years old	3 - 6 years old
Average duration of blockade (standard deviation)	12 months (± 24 days)	11 months (± 93 days)

In bitches where gonadal function has been successsfully prevented for a period of 12 months, then a second treatment may be administered at that time for continued prevention of oestrus. There are no data available for animals treated on more than two occasions.

9. ADVICE ON CORRECT ADMINISTRATION

Gonazon should be injected subcutaneously, in the ventral anterior abdominal wall, in the region of the umbilicus, using aseptic technique.

ADMINISTRATION:

1. Position the bitch on her back. Prepare a small area (*e.g.* 4 cm²) of the ventral anterior abdominal/umbilical region for an aseptic procedure (Fig. 1).
2. Open the foil pouch using the pre-cut incision to remove the sterile injection device.
3. Remove the needle cap. Unlike liquid injections, there is no need to remove air bubbles as attempts to do so may displace the implant from the needle.
4. Using aseptic technique, raise a small piece of skin in the region of the dog's umbilicus. With the bevel of the needle facing upwards, insert the needle at a 30 degree angle to the tented skin in a single motion (Fig. 2).
5. Take care to avoid penetrating the abdominal wall musculature or fat tissue.
6. With your free hand, use the thumb grip to hold the injection device in position, and depress the plunger as far as it can go. This retracts the needle and withdraws it, leaving the implant beneath the skin (Fig. 3). Withdraw the needle from the skin.
7. Ensure that the administration site is clean and dry. Instruct the owner to keep the administration site clean and dry for 24 hours. Record the date of treatment in the clinical records of the animal.

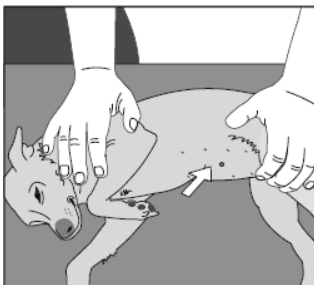

Fig.1

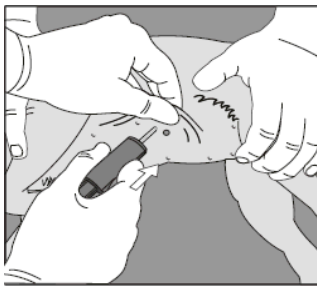

Fig.2

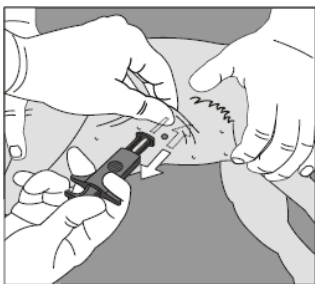

Fig.3

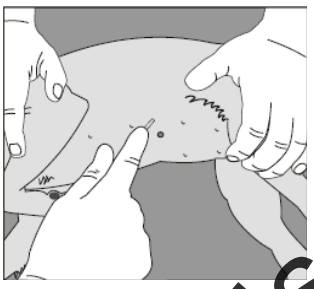

Fig.4

REMOVAL:

Chemical restraint (sedation and/or general anaesthesia) may be required for implant removal. Position the dog as described for administration of the implant.

1. Locate the implant by gentle digital palpation of the administration site. Prepare the site for an aseptic technique.
2. After adequate (local) anaesthesia is present, apply gentle digital pressure to the far end of the implant. Make a stab incision, approximately 5 mm long, along the elevated near end of the implant. Push the implant gently towards the stab incision. If necessary, dissect away any fibrous tissue to free the implant. Grasp it with forceps and remove.
3. Instruct the owner to keep the administration site clean and dry for 24 hours.

Treatment in proestrus will not suppress that particular heat (proestrus and oestrus).

In adult bitches, heat is commonly induced in the first month following the first administration of the implant. The frequency of induced heat is lower when the first treatment is administered in metoestrus (32%) than in anoestrus (84%). Therefore, the first treatment should preferably be administered in metoestrus. The incidence of induced heat following administration of a repeat treatment to bitches that have not shown signs of oestrus following a previous administration of the product is low (estimated to be 8%).

The risk of inducing a fertile heat is low in metoestrus (5%). Administration of Gonazon at other stages of the cycle may induce heat that may be fertile. If a bitch becomes pregnant following induced heat, embryonic resorption or abortion may occur. Therefore, if heat is observed, contact with male dogs should be prevented until all signs of heat (vulvar swelling, bleeding and attractiveness to male dogs) cease.

Induced heat is not observed if treatment is started before puberty. In addition, the frequency of induced heat is lower in younger bitches than in older bitches.

A proportion of bitches that show induced heat may subsequently develop pseudopregnancy. However, based on field trial data, the incidence of pseudopregnancy in treated bitches is not greater than in control (untreated) bitches.

The product when administered at the recommended treatment dose is ineffective in bitches aged 7 years or older.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Do not use after the expiry date which is stated on the label 'EXP'
Do not store above 25°C.

12. SPECIAL WARNING(S)

The implant may not be retained in a proportion (1.2%) of treated bitches. If the implant cannot be palpated in the month following administration, the owner is encouraged to seek veterinary advice as efficacy cannot be ensured in these cases.

At the end of a one year treatment, it may not be possible to locate and remove the implant in approximately 10% of cases. To minimise this problem, caution needs to be exercised to ensure that the implant is administered by subcutaneous injection, particularly in dogs with pronounced depots of subcutaneous fat. Inability to locate and remove Gonazon will not have serious effects on the general health of the dog. However, the timing of return to heat cannot be predicted.

Following a single administration, return to ovarian activity after implant removal may take longer in bitches treated before puberty (average 255 days, range 36-429 days) than in adult bitches (average 68 days, range 12 to 264 days). A large proportion (68%) of the first heat after a single treatment in adult bitches were non-ovulatory. In addition following a repeat treatment, the timing of a return to heat cannot be accurately predicted. No data are available on repeat treatments in prepubertal bitches.

Accidental ingestion of the implant by the dog will not affect its health, since the oral bio-availability of GnRH agonists is very low.

The use is not recommended during pregnancy and lactation. Laboratory studies have shown that administration of the product during early pregnancy in the bitch is unlikely to affect that pregnancy (that is, pregnancy will be carried to full term with the birth of viable pups).

Personal protective equipment, consisting of gloves, should be worn when handling the veterinary medicinal product.

Avoid accidental self-injection. In the event of accidental self-administration of the implant, seek medical advice immediately and show the package leaflet or the label to the physician.

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

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

13.06.2008

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu/.

15. OTHER INFORMATION

An individual carton box contains a single disposable injection device, preloaded inside a hypodermic needle covered with a protective cap.