ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oncept IL-2 lyophilisate and solvent for suspension for injection for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, each dose of 1 ml contains:

Active substance:

Feline interleukin-2 recombinant canarypox virus (vCP1338)..... $\geq 10^{6.0}$ $EAID^{*}_{50}$
*ELISA infectious dose 50%.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension for injection.
Lyophilisate: whitish homogeneous pellet.
Solvent: clear colourless liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Cats.

4.2 Indications for use, specifying the target species

Immunotherapy to be used in addition to surgery and radiotherapy in cats with fibrosarcoma (2-5 cm diameter) without metastasis or lymph node involvement in order to reduce the risk of relapse and to increase the time to relapse (local recurrence or metastasis). This was demonstrated in a field trial over a period of 2 years.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Use of the recommended mode of administration in 5 injection points is important for achieving efficacy of the product; injection in 1 point may lead to reduced efficacy (see section 4.9).
Efficacy has only been tested in conjunction with surgery and radiotherapy; therefore the treatment should be conducted according to treatment course described in section 4.9.
Efficacy has not been tested in cats with metastasis or lymph node involvement.
As safety and efficacy of repetition of the treatment to treat fibrosarcoma recurrence have not been investigated, repetition of the treatment should be considered by the veterinarian taking into account the benefit-risk balance.
Efficacy of the treatment has not been investigated beyond 2 years following treatment.

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

Canarypox recombinants are known to be safe for humans. Mild local and/or systemic adverse reactions related to the injection itself may be observed transitorily. Moreover feline IL-2 has been shown to have very low biological activity on human leukocytes compared to human IL-2. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

A moderate local reaction (pain on palpation, swelling, scratching) occurred very commonly in safety studies. It usually disappeared spontaneously within 1 week at most.
Transient apathy and hyperthermia (above 39.5 °C) occurred commonly in field studies.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this immunological veterinary medicinal product when used with any other veterinary medicinal product. A decision to use this immunological veterinary medicinal product before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

4.9 Amounts to be administered and administration route

Subcutaneous use.

After reconstitution of the lyophilisate with the solvent, shake gently and administer five injections (each approximately 0.2 ml) around the tumour excision site: one injection at each corner and one injection at the centre of a 5 cm x 5 cm square centred on the middle of the surgical scar.

Treatment course: 4 administrations at 1-week intervals (day 0, day 7, day 14, day 21) followed by 2 administrations at 2-week intervals (day 35, day 49).
Start the treatment course the day before radiation therapy, preferably within one month after surgical excision.

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

After the administration of an overdose (10 doses), transient moderate to marked hyperthermia, as well as local reactions (swelling, erythema or slight pain, and in some cases, heat at the injection site) may occur.

4.11 Withdrawal period(s)

Not applicable.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antineoplastic and immunomodulating agents, other immunostimulants.
ATC-vet code: QL03AX90.

The vaccine strain vCP1338 is a recombinant canarypox virus expressing feline interleukin-2 (IL-2). The virus expresses the IL-2 gene at the inoculation site, but does not replicate in the cat.
Oncept IL-2 injected into the tumour bed thus delivers *in situ* a low dose of feline interleukin-2, which stimulates antitumour immunity while avoiding toxicity associated with systemic treatment. Specific mechanisms by which immunostimulation induces anti-tumoural activity are not known.

In a randomized clinical study, cats from different origins presenting a fibrosarcoma without metastasis or lymph node involvement were included in two groups, one receiving the reference treatment – surgery and radiotherapy – and the other receiving Oncept IL-2 in addition to surgery and radiotherapy. After two years of study follow-up, Oncept IL-2 treated cats showed a longer median time to relapse (above 730 days) compared to control cats (287 days). Oncept IL-2 treatment reduced the risk of relapse, from 6 months after the start of treatment, by approximately 56% after 1 year and 65% after 2 years.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lyophilisate:
Sucrose
Collagen hydrolysate
Casein hydrolysate
Sodium chloride
Disodium phosphate dihydrate
Potassium dihydrogen phosphate.

Solvent:
Water for injections.

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product, except the solvent supplied for use with the veterinary medicinal product.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: use immediately after reconstitution.

6.4 Special precautions for storage

Store and transport refrigerated (2 °C-8 °C).
Store in the original package in order to protect from light.
Do not freeze.

6.5 Nature and composition of immediate packaging

Type I glass vial with a butyl elastomer closure, sealed with an aluminium cap.

Cardboard box of 6 vials of 1 dose of lyophilisate and 6 vials of 1 ml of solvent.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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.

7. MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
GERMANY

8. MARKETING AUTHORISATION NUMBERS

EU/2/13/150/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03/05/2013
Date of last renewal: 20/03/2018

10. DATE OF REVISION OF THE TEXT

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

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Boehringer Ingelheim Animal Health France SCS
Laboratoire Porte des Alpes
Rue de l'Aviation
69800 Saint Priest
France

Name and address of the manufacturer responsible for batch release

Boehringer Ingelheim Animal Health France SCS
Laboratoire Porte des Alpes
Rue de l'Aviation
69800 Saint Priest
France

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box of 6 vials of lyophilisate and 6 vials of solvent

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oncept IL-2 lyophilisate and solvent for suspension for injection for cats

2. STATEMENT OF ACTIVE SUBSTANCES

Feline interleukin-2 recombinant canarypox virus (vCP1338) .....$\geq 10^{6.0}$ $EAID_{50}$

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension for injection

4. PACKAGE SIZE

Lyophilisate: 6 x 1 dose
Solvent: 6 x 1 ml

5. TARGET SPECIES

Cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Use immediately after reconstitution.

11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated. Store in the original package in order to protect from light.
Do not freeze.

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

Disposal: read package leaflet.

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

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
GERMANY

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/150/001

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Lyophilisate vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oncept IL-2 lyophilisate

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

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

1 dose

4. ROUTE(S) OF ADMINISTRATION

SC
Read the package leaflet before use.

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Solvent vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Solvent for Oncept IL-2

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

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

1 ml

4. ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Oncept IL-2 lyophilisate and solvent for suspension for injection for cats

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

Marketing authorisation holder:
Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
GERMANY

Manufacturer responsible for batch release:
Boehringer Ingelheim Animal Health France SCS
Laboratoire Porte des Alpes
Rue de l'Aviation
69800 Saint Priest
France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oncept IL-2 lyophilisate and solvent for suspension for injection for cats

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

After reconstitution, each dose of 1 ml contains:

Feline interleukin-2 recombinant canarypox virus (vCP1338) ..... $\geq 10^{6.0}$ EAID*$_{50}$
*ELISA infectious dose 50%.

Lyophilisate: whitish homogeneous pellet.
Solvent: clear colourless liquid.

4. INDICATION(S)

Immunotherapy to be used in addition to surgery and radiotherapy in cats with fibrosarcoma (2-5 cm diameter) without metastasis or lymph node involvement in order to reduce the risk of relapse and to increase the time to relapse (local recurrence or metastasis). This was demonstrated in a field trial over a period of 2 years.

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

A moderate local reaction (pain on palpation, swelling, scratching) occurred very commonly in safety studies. It usually disappeared spontaneously within 1 week at most.
Transient apathy and fever (above 39.5 °C) occurred commonly in field studies.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s)) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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

7. TARGET SPECIES

Cats.

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

Subcutaneous use.

After reconstitution of the lyophilisate with the solvent, shake gently and administer five injections (each approximately 0.2 ml) around the tumour excision site: one injection at each corner and one injection at the centre of a 5 cm x 5 cm square centred on the middle of the surgical scar.

Treatment course: 4 administrations at 1-week intervals (day 0, day 7, day 14, day 21) followed by 2 administrations at 2-week intervals (day 35, day 49).
Start the treatment course the day before radiation therapy, preferably within one month after surgical excision.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store and transport refrigerated (2 °C-8 °C).
Store in the original package in order to protect from light.
Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP.
After reconstitution use immediately.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Use of the recommended mode of administration in 5 injection points is important for achieving efficacy of the product; injection in 1 point may lead to reduced efficacy (see section “Dosage for each species, route and method of administration”).
Efficacy has only been tested in conjunction with surgery and radiotherapy; therefore the treatment should be conducted according to treatment course described in section “Dosage for each species, route and method of administration”.
Efficacy has not been tested in cats with metastasis or lymph node involvement.
As safety and efficacy of repetition of the treatment to treat fibrosarcoma recurrence have not been investigated, repetition of the treatment should be considered by the veterinarian taking into account the benefit-risk balance.
Efficacy of the treatment has not been investigated beyond 2 years following treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Canarypox recombinants are known to be safe for humans. Mild local and/or systemic adverse reactions related to the injection itself may be observed transitorily. Moreover feline IL-2 has been shown to have very low biological activity on human leukocytes compared to human IL-2. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Overdose (symptoms, emergency procedures, antidotes):
After the administration of an overdose (10 doses), transient moderate to marked hyperthermia, as well as local reactions (swelling, redness or slight pain, and in some cases, heat at the injection site) may occur.

Interaction with other medicinal products and other forms of interaction:
No information is available on the safety and efficacy of this immunological veterinary medicinal product when used with any other veterinary medicinal product. A decision to use this immunological veterinary medicinal product before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Incompatibilities:
Do not mix with any other veterinary medicinal product, except the solvent supplied for use with the veterinary medicinal 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 product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

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

15. OTHER INFORMATION

The vaccine strain vCP1338 is a recombinant canarypox virus expressing feline interleukin-2 (IL-2). The virus expresses the IL-2 gene at the inoculation site, but does not replicate in the cat.
Oncept IL-2 injected into the tumour bed thus delivers *in situ* a low dose of feline interleukin-2, which stimulates antitumour immunity while avoiding toxicity associated with systemic treatment.
Specific mechanisms by which immunostimulation induces anti-tumoural activity is not known.

In a randomized clinical study, cats from different origins presenting a fibrosarcoma without metastasis or lymph node involvement were included in two groups, one receiving the reference treatment – surgery and radiotherapy – and the other receiving Oncept IL-2 in addition to surgery and radiotherapy. After two years of study follow-up, Oncept IL-2 treated cats showed a longer median time to relapse (above 730 days) compared to control cats (287 days). Oncept IL-2 treatment reduced the risk of relapse, from 6 months after the start of treatment, by approximately 56% after 1 year and 65% after 2 years, compared to the control group.

Cardboard box containing 6 vials of 1 dose of lyophilisate and 6 vials of 1 ml of solvent.