**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

INCURIN 1 mg tablet

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: estriol 1 mg/tablet

For a full list of excipients, see section 6.1

## 3. PHARMACEUTICAL FORM

Round single-scored tablets

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Dogs (bitches).

### 4.2 Indications for use, specifying the target species

The treatment of hormone-dependent urinary incontinence due to sphincter mechanism incompetence in ovariohysterectomised bitches.

### 4.3 Contraindications

Do not use in intact bitches, as the efficacy has only been established in ovariohysterectomised bitches.
Animals showing a polyuria-polydipsia should not be treated with Incurin.
The use of Incurin is contraindicated during pregnancy, lactation and in animals younger than 1 year.

### 4.4 Special warnings for each target species

High doses of oestrogen may have a tumour-promoting effect in target organs with oestrogen receptors (mammary glands).

### 4.5 Special precautions for use

**Special precautions for use in animals**
In case of oestrogenic effects, the dose should be lowered.

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

Not applicable.

### 4.6 Adverse reactions (frequency and seriousness)

Oestrogenic effects such as swollen vulva, swollen mammary glands and/or attractiveness to males and vomiting have been observed at the highest recommended dose of 2 mg per dog. The incidence is about 5-9 %. These effects are reversible after lowering the dose.
In rare cases vaginal bleeding occurred. In rare cases development of alopecia has also been observed.

### 4.7 Use during pregnancy, lactation or lay

Do not use this product during pregnancy or lactation. See also 4.3 Contraindications.

### 4.8 Interaction with other medicinal products and other forms of interaction

None known.

### 4.9 Amount(s) to be administered and administration route

For oral administration.
A relationship between final effective dose and body weight has not been established and therefore the dose has to be determined for each dog on an individual basis.
The following dosing schedule is advised: start treatment with 1 tablet (1 mg estriol) every day. If treatment is successful, lower the dose to half a tablet a day. If treatment is not successful, increase the dose to 2 tablets a day to be given in one dose. Some dogs do not need daily treatment; treatment every other day may be tried, once the effective daily dose has been established.
The minimum dose given should not be less than 0.5 mg per dog per day. Ensure the dose used to achieve the therapeutic effect is as low as possible. Do not use more than 2 tablets per dog per day. If no response to treatment is obtained the diagnosis should be reconsidered in order to investigate other causes for the incontinence such as neurological disorders, bladder neoplasia, etc.
Animals should be re-examined every 6 months during treatment.

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

In case of overdose typical oestrogen effects may occur. These effects are reversible after lowering the dose.

### 4.11 Withdrawal period(s)

Not applicable.

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: estrogens, ATCvet code: QG03CA04.

### 5.1 Pharmacodynamic properties

Estriol is a short-acting natural oestrogen. In ovarioectomised female dogs it has a beneficial effect on urinary incontinence. In the target animal safety study and the clinical trials, including long-term treatment, no signs of bone marrow suppression were observed. This is probably due to the short-acting oestrogenic character of estriol.

### 5.2 Pharmacokinetic particulars

After oral administration Estriol is nearly completely absorbed from gastrointestinal tract. Nearly the whole Estriol is bound to Albumin in Plasma. Estriol is excreted in conjugated from via the urine.
After oral administration of multiple doses no accumulation occurs.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Amylopectin
Potato starch
Magnesium stearate
Lactose

### 6.2 Incompatibilities

None.

### 6.3 Shelf life

3 years.

### 6.4 Special precautions for storage

Do not store above 30°C.

### 6.5 Nature and composition of immediate packaging

Blister package of clear PVC film backed by aluminium foil provided with heat seal coating (vinyl copolymer) on the side in contact with the tablets. One blister contains 30 tablets.

Pack size: carton box with 1 blister

### 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.

## 7 MARKETING AUTHORISATION HOLDER

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

## 8 MARKETING AUTHORISATION NUMBER(S)

EU/2/00/018/001

## 9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: March 2000
Date of last renewal: March 2010

## 10 DATE OF REVISION OF THE TEXT

## 11 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) of the biological active substance(s)

Aspen Oss. B.V.
Kloosterstraat 6
5349 AB Oss
The Netherlands

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

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

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

To be supplied only on veterinary prescription

## 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

Not applicable.

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARTON BOX**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

INCURIN 1 mg tablet
Estriol

## 2. STATEMENT OF ACTIVE AND OTHER SUBTANCES

Active substance: estriol 1 mg/tablet

## 3. PHARMACEUTICAL FORM

Tablet.

## 4. PACKAGE SIZE

Carton box with 1 blister. Each blister contains 30 tablets.

## 5. TARGET SPECIES

Dog.

## 6. INDICATION(S)

Treatment of hormone-dependent urinary incontinence due to sphincter mechanism incompetence in female dogs.

## 7. METHOD AND ROUTE OF ADMINISTRATION

For oral administration.
Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD

Not applicable.

## 9. SPECIAL WARNINGS, IF NECESSARY

Not applicable.

## 10. EXPIRY DATE

Exp (Month / year)

## 11. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.

## 12. SPECIFIC 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.

## 13. THE WORDS "FOR ANIMAL TREATMENT ONLY"

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

## 16. MARKETING AUTHORISATION NUMBER(S)

EU/2/00/018/001

## 17. MANUFACTURER'S BATCH NUMBER

Batch number.

**MINIMUM PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

**BLISTER**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

INCURIN 1 mg tablet.
Estriol

## 2. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

## 3. EXPIRY DATE

(Month / year)

## 4. BATCH NUMBER

Batch number.

## 5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

**B. PACKAGE LEAFLET**

**PACKAGE LEAFLET**

**INCURIN 1 mg tablet**

## 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

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

INCURIN 1 mg tablet
Estriol

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

Active substance: estriol 1 mg/tablet

Round single-scored tablets.

## 4. INDICATION

Incurin is indicated for the treatment of hormone-dependent urinary incontinence due to sphincter mechanism incompetence in female dogs.

## 5. CONTRAINDICATIONS

Do not use in intact bitches, as the efficacy has only been established in ovariohysterectomised bitches.
Animals showing a polyuria-polydipsia should not be treated with Incurin.
The use of Incurin is contraindicated during pregnancy, lactation and in animals younger than 1 year.

## 6. ADVERSE REACTIONS

Mild, oestrogenic effects such as swollen vulva, swollen teats and/or attractiveness for males have been observed at the high dose of 2 mg. These effects are reversible after lowering the dose. Further, in some dogs, symptoms of nausea were observed. Because of its short-acting oestrogenic properties, Incurin does not induce bone marrow suppression in the dog.
In rare cases vaginal bleeding occurred. In rare cases development of alopecia has also been observed.

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

## 7. TARGET SPECIES

Dog.

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

Incurin is intended for once daily oral administration.
Since there exists no relation between the final effective dose and the body weight, a fixed dose per kg body weight is not feasible. The dose has to be fixed for each dog on an individual basis. The following dosing schedule is advised: start treatment with 1 tablet every day. If treatment is successful lower the dose to half a tablet a day. If treatment is not successful increase the dose to 2 tablets a day. Some dogs do not need daily treatment; treatment every other day may be tried once the effective daily dose has been established.

## 9. ADVICE ON CORRECT ADMINISTRATION

Not applicable.

## 10. WITHDRAWAL PERIOD

Not applicable.

## 11. SPECIAL STORAGE CONDITIONS

Keep out of the reach and sight of children.

Do not store above 30°C.
Do not use after the expiry date which is stated on the label after Exp.

## 12. SPECIAL WARNINGS

High doses of oestrogen may have a tumour-promoting effect in target organs with oestrogen receptors (mammary glands).
In case of overdose typical oestrogen effects may occur. These effects are reversible after lowering the dose.

## 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

## 15. OTHER INFORMATION

Each push-through strip contains 30 tablets. Each strip is packed in a carton box.

Oestriol is a short-acting natural oestrogen. In the incontinent female dog it has a beneficial effect on the urinary incontinence. Upon oral administration a steady state is reached after the second treatment day and no accumulation occurs after multiple dosing. Because of its short acting action, oestriol does not induce bone marrow suppression in the dog.

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