ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PGF Veyx forte 0.250 mg/ml solution for injection for cattle and pigs
PGF Veyx 0.250 mg/ml solution for injection for cattle and pigs (France, Italy)
Cloprostenol Veyx forte 0.250 mg/ml solution for injection for cattle and pigs (Poland)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution for injection contains:

Active substance:
Cloprostenol 0.250 mg (corresponding to 0.263 mg cloprostenol sodium)

Excipients:
Chlorocresol 1.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless aqueous solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (heifers, cows) and pigs (sows)

4.2 Indications for use, specifying the target species

Cattle (heifers, cows):

- To schedule the time of oestrous and ovulation and for cycle synchronization in animals with an ovulatory cycle when applied during the diestrus (induction of oestrus in non-detected oestrus, synchronisation of oestrus)
- Treatment of anoestrus and uterine disorders caused by a progesterone-induced oestrous cycle blockade (induction of oestrous in anoestrus, endometritis, pyometra, corpus luteal cysts, follicular luteal cysts, shortening of the sexual rest period)
- Induction of abortion up to day 150 of pregnancy
- Expulsion of mummified foetuses
- Induction of parturition

Pigs (sows):

- Induction or synchronisation of farrowing from day 114 of pregnancy onwards (day 1 of pregnancy is the last day of insemination).

4.3 Contraindications

- Do not use for intravenous administration
- Do not use in pregnant animals where the induction of abortion or parturition is not intended
- Do not use in case of spastic diseases of the respiratory tract and gastrointestinal tract
- Do not use in cases of hypersensitivity to the active substance or to any of excipients

4.4 Special warnings for each target species

None

4.5 Special precautions for use

Special precautions for use in animals

To reduce the risk of anaerobic infections care should be taken to avoid injection through contaminated areas of skin. Clean and disinfect injection sites thoroughly before application.

Pigs:
Use only if the cover dates are known. Too early an administration could adversely affect the viability of the piglets. This is the case when the injection is given more than 2 days before the average gestation period of the stock. Day 1 of pregnancy is the last day of insemination. The gestation period is generally 111-119 days.

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

- This product must be handled carefully to avoid accidental self-injection or contact with the skin or mucous membranes of the user.
- Prostaglandins of the F2α type may be absorbed through the skin and may cause bronchospasm or miscarriage.
- Pregnant women, women in childbearing age, asthmatics and people with other respiratory tract diseases should wear waterproof gloves during administration of the product.
- Accidental spillage on the skin should be washed off immediately with soap and water.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Should respiratory distress result from accidental inhalation or injection, a rapid acting bronchodilator, e.g. isoprenaline or salbutamol by inhalation is indicated.

4.6 Adverse reactions (frequency and seriousness)

Anaerobic infections may occur if anaerobic bacteria are introduced into the tissue by the injection, in particular following intramuscular injection.

Cattle:
When used for induction of parturition, the incidence of retained placenta may be increased depending on the time of treatment. In very rare cases, anaphylactic-type reactions can be observed which might be life threatening and require rapid medical care.

Pigs:
The abnormal behaviour that might occur in pigs immediately after treatment, when the drug has been used to induce parturition, is similar to that of sows before normal birth and normally subsides within one hour.

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

Do not use in pregnant animals when abortion or induction of parturition is not intended.
Safety of the product has not been established during lactation.
Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent use of oxytocin and Cloprostenol increases the effects on the uterus.
Do not use in animals being treated with non-steroidal anti-inflammatories, as the synthesis of endogenous prostaglandins is inhibited.

4.9 Amounts to be administered and administration route

For intramuscular injection in cattle (heifers, cows).
For deep intramuscular injection in pigs (sows) (with a needle at least 4 cm long).

Cattle (heifers, cows): 0.5 mg Cloprostenol/animal corresponding to 2.0 ml of the product/animal

In order to synchronise oestrus in a cattle herd, it is recommended that the product is administered on two occasions with an 11-day interval between treatments.

Pigs (sows): 0.175 mg Cloprostenol/animal corresponding to 0.7 ml of the product/animal
Use automatic syringe equipment for the 50 ml vials.

Single administration.

The rubber stopper of the vial may be safely punctured up to 25 times. Otherwise, automatic syringe equipment, or a suitable draw-off needle, should be used for the 50 ml vials to avoid excessive puncturing of the closure.

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

In case of overdose the following symptoms may occur:
Increased heart rate, increased respiratory rate, bronchoconstriction, increased rectal temperature, increased defecation and urination, salivation, nausea and vomiting.
No antidotes are available.

4.11 Withdrawal period(s)

Cattle, pigs (meat and offal): 2 days
Cattle (milk): zero hours

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: prostaglandin-$F_{2\alpha}$-agonist
ATCvet code: QG02AD90

Cloprostenol belongs to the group of prostaglandin-$F_{2\alpha}$-agonists, which exert a luteolytic effect dependent on species and time of treatment. Furthermore, this group of substances has a contractile effect on the smooth muscles (uterus, gastro-intestinal tract, respiratory tract, vascular system).

Treatment during diestrus or in the case of persistent corpus luteum causes luteolysis. The associated removal of the negative feed-back mechanism induced by progesterone leads in animals with cyclic ovarian function to a premature onset of heat and ovulation.
Cloprostenol produces a 200- to 400-fold luteolytic effect compared to prostaglandin-$F_{2\alpha}$; however, the effect on the smooth muscles appears to be equally strong.

5.2 Pharmacokinetic particulars

Peak plasma concentrations were observed within 15 minutes to 2 hours after intramuscular injection of Cloprostenol in cattle and pigs. The subsequent rapid elimination phase is characterised by a half-life from 1 to 3 hours, with a subsequent phase of slow elimination over a period of up to 48 hours, with a half-life of 28 hours.
Cloprostenol is distributed evenly throughout the tissues. Excretion via the faeces and urine is virtually equal. Less than 0.4% of the applied dose in cattle is eliminated via the milk. Maximum concentrations are measured approx. 4 hours post application.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol
Citric acid monohydrate
Sodium chloride
Sodium hydroxide (for pH-adjustment)
Sodium citrate
Water for injections

6.2 Major 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: 4 years
Shelf life after first opening the immediate packaging: 28 days

6.4. Special precautions for storage

Do not store above 25°C.
Protect from light.
Keep the vial in the outer carton.

6.5 Nature and composition of immediate packaging

Vial of colourless glass, type I, with a fluorinated bromobutyl stopper and an aluminium cap;
1 vial (10 ml) in a cardboard box.
1 vial (20 ml) in a cardboard box.
1 vial (50 ml) in a cardboard box.
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.

7. MARKETING AUTHORISATION HOLDER

Veyx-Pharma GmbH
Söhreweg 6
34639 Schwarzenborn
Germany

8. MARKETING AUTHORISATION NUMBER(S)

……..

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

……..

10. DATE OF REVISION OF THE TEXT

……..

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

for 10 ml / 20 ml / 50 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PGF Veyx forte 0.250 mg/ml solution for injection for cattle and pigs
PGF Veyx 0.250 mg/ml solution for injection for cattle and pigs (France, Italy)
Cloprostenol Veyx forte 0.250 mg/ml solution for injection for cattle and pigs (Poland)
Cloprostenol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml solution for injection contains:
Active substance(s):
Cloprostenol 0.250 mg (corresponding to 0.263 mg cloprostenol sodium)
Excipients:
Chlorocresol 1.0 mg

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

1 x 10 ml / 1 x 20 ml / 1 x 50 ml

5. TARGET SPECIES

Cattle (heifers, cows) and pigs (sows)

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For intramuscular injection in cattle (heifers, cows).
For deep intramuscular injection in pigs (sows).
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Cattle, pigs (meat and offal): 2 days
Cattle (milk): zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

Expiry date: month/year
Once broached, use by:
Shelf life after first broaching the vial: 28 days

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Protect from light.
Keep the vial in the outer carton.

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

Veyx-Pharma GmbH
Söhreweg 6
34639 Schwarzenborn
Germany

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch number:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PGF Veyx forte 0.250 mg/ml solution for injection for cattle and pigs
PGF Veyx 0.250 mg/ml solution for injection for cattle and pigs (France, Italy)
Cloprostenol Veyx forte 0.250 mg/ml solution for injection for cattle and pigs (Poland)
Cloprostenol

2. QUANTITY OF THE ACTIVE SUBSTANCE

3. CONTENTS BY VOLUME

10 ml

4. ROUTE(S) OF ADMINISTRATION

For intramuscular injection in cattle (heifers, cows).
For deep intramuscular injection in pigs (sows).

5. WITHDRAWAL PERIOD

Withdrawal period:
Cattle, pigs (meat and offal): 2 days
Cattle (milk): zero hours

6. BATCH NUMBER

Batch number:

7. EXPIRY DATE

Expiry date: month/year
Once broached, use by:

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

20 ml / 50 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PGF Veyx forte 0.250 mg/ml solution for injection for cattle and pigs
PGF Veyx 0.250 mg/ml solution for injection for cattle and pigs (France, Italy)
Cloprostenol Veyx forte 0.250 mg/ml solution for injection for cattle and pigs (Poland)
Cloprostenol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml solution for injection contains:
Active substance(s):
Cloprostenol 0.250 mg (corresponding to 0.263 mg cloprostenol sodium)
Excipients:
Chlorocresol 1.0 mg

3. PHARMACEUTICAL FORM

4. PACKAGE SIZE

20 ml / 50 ml

5. TARGET SPECIES

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For intramuscular injection in cattle (heifers, cows).
For deep intramuscular injection in pigs (sows).
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Cattle, pigs (meat and offal): 2 days
Cattle (milk): zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

Expiry date: month/year
Once broached, use by:
Shelf life after first broaching the vial: 28 days

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Protect from light.
Keep the vial in the outer carton.

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

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

Veyx-Pharma GmbH
Söhreweg 6
34639 Schwarzenborn
Germany

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER’S BATCH NUMBER

Batch number:

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

PGF Veyx forte 0.250 mg/ml solution for injection for cattle and pigs
PGF Veyx 0.250 mg/ml solution for injection for cattle and pigs (France, Italy)
Cloprostenol Veyx forte 0.250 mg/ml solution for injection for cattle and pigs (Poland)

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:

Veyx-Pharma GmbH
Söhreweg 6
34639 Schwarzenborn
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

PGF Veyx forte 0.250 mg/ml solution for injection for cattle and pigs
PGF Veyx 0.250 mg/ml solution for injection for cattle and pigs (France, Italy)
Cloprostenol Veyx forte 0.250 mg/ml solution for injection for cattle and pigs (Poland)
Cloprostenol

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

The product is a clear, colourless aqueous solution for injection containing:
Active substance:
Cloprostenol 0.250 mg/ml (corresponding to 0.263 mg/ml cloprostenol sodium)
Excipients:
Chlorocresol 1.0 mg/ml

4. INDICATION(S)

Cattle (heifers, cows):

- To schedule the time of oestrous and ovulation and for cycle synchronization in animals with an ovulatory cycle when applied during the diestrus (induction of oestrus in non-detected oestrus, synchronisation of oestrus)
- Treatment of anoestrus and uterine disorders caused by a progesterone-induced oestrous cycle blockade (induction of oestrous in anoestrus, endometritis, pyometra, corpus luteal cysts, follicular luteal cysts, shortening of the sexual rest period)
- Induction of abortion up to day 150 of pregnancy
- Expulsion of mummified foetuses
- Induction of parturition

Pigs (sows):

- Induction or synchronisation of farrowing from day 114 of pregnancy onwards (day 1 of pregnancy is the last day of insemination).

5. CONTRAINDICATIONS

- Do not use for intravenous administration
- Do not use in pregnant animals where the induction of abortion or parturition is not intended
- Do not use in case of spastic diseases of the respiratory tract and gastrointestinal tract
- Do not use in cases of hypersensitivity to the active substance or to any of excipients

6. ADVERSE REACTIONS

Anaerobic infections may occur if anaerobic bacteria are introduced into the tissue by the injection, in particular following intramuscular injection.
Cattle:
When used for induction of parturition, the incidence of retained placenta may be increased depending on the time of treatment.
In very rare cases, anaphylactic-type reactions can be observed which might be life threatening and require rapid medical care.

Pigs:
The abnormal behaviour that might occur in pigs immediately after treatment, when the drug has been used to induce parturition, is similar to that of sows before normal birth and normally subsides within one hour.

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)

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

Cattle (heifers, cows) and pigs (sows)

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

For intramuscular injection in cattle (heifers, cows).
For deep intramuscular injection in pigs (sows) (with a needle at least 4 cm long).

Cattle (heifers, cows): 0.5 mg Cloprostenol/animal corresponding to 2.0 ml of the product/animal

In order to synchronise oestrus in a cattle herd, it is recommended that the product is administered on two occasions with an 11-day interval between treatments.

Pigs (sows): 0.175 mg Cloprostenol/animal corresponding to 0.7 ml of the product/animal
Use automatic syringe equipment for the 50 ml vials.

Single administration.

The rubber stopper of the vial may be safely punctured up to 25 times. Otherwise, automatic syringe equipment, or a suitable draw-off needle, should be used for the 50 ml vials to avoid excessive puncturing of the closure.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIOD

Cattle, pigs (meat and offal): 2 days
Cattle: milk:zero hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not store above 25°C.
Protect from light.
Keep the vial in the outer carton.
Do not use after the expiry date stated on the vial and carton.
Shelf life after first opening the immediate packaging: 28 days
When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package insert, the date on which any product remaining in the vial should be discarded should be worked out. This discard date should be written in the space provided on the label.

12. SPECIAL WARNING(S)

Special warnings for each target species:
None.
Special precautions for use:
Special precautions for use in animals:
To reduce the risk of anaerobic infections care should be taken to avoid injection through contaminated areas of skin. Clean and disinfect injection sites thoroughly before application.
Pigs:
Use only if the cover dates are known. Too early an administration could adversely affect the viability of the piglets. This is the case when the injection is given more than 2 days before the average gestation period of the stock. Day 1 of pregnancy is the last day of insemination. The gestation period is generally 111-119 days.

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

- This product must be handled carefully to avoid accidental self-injection or contact with the skin or mucous membranes of the user.
- Prostaglandins of the F2α type may be absorbed through the skin and may cause bronchospasm or miscarriage.
- Pregnant women, women in childbearing age, asthmatics and people with other respiratory tract diseases should wear waterproof gloves during administration of the product.
- Accidental spillage on the skin should be washed off immediately with soap and water.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Should respiratory distress result from accidental inhalation or injection, a rapid acting bronchodilator, e.g. isoprenaline or salbutamol by inhalation is indicated.

Use during pregnancy, lactation or lay:
Do not use in pregnant animals when abortion or induction of parturition is not intended.
Safety of the product has not been established during lactation.
Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction
Concurrent use of oxytocin and Cloprostenol increases the effects on the uterus.
Do not use in animals being treated with non-steroidal anti-inflammatories, as the synthesis of endogenous prostaglandins is inhibited.

Overdose (symptoms, emergency procedures, antidotes), if necessary:
In case of overdose the following symptoms may occur:

Increased heart rate, increased respiratory rate, bronchoconstriction, increased rectal temperature, increased defecation and urination, salivation, nausea and vomiting.
No antidotes are available.

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

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

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

15. OTHER INFORMATION

1 vial (10 ml) in a cardboard box
1 vial (20 ml) in a cardboard box
1 vial (50 ml) in a cardboard box

Not all pack sizes may be marketed.