

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonavet Veyx 50 µg/ml solution for injection for cattle, pigs and horses (DE, AT, BE, BG, CZ, EL, ES, FR, HU, HR, IS, IT, LT, LU, LV, NL, PT, RO, SI, SK)

Gonavet Veyx 50 micrograms/ml solution for injection for cattle, pigs and horses (IE/UK/EE)

Gonavet Veyx Depherelin 50 micrograms/ml solution for injection for cattle, pigs and horses (PL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1.0 ml contains:

Active substance:

Gonadorelin[6-D-Phe] 50 micrograms (equivalent to 52.4 micrograms Gonadorelin[6-D-Phe] acetate)

Excipients:

Chlorocresol 1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (cows, heifers), pigs (sows, gilts), horses (mares)

4.2 Indications for use, specifying the target species

Control and stimulation of reproduction in cattle and pigs. Treatment of ovarian-related fertility disorders or dysfunctions in cattle and horses.

Cattle (cows, heifers):

- Ovulation induction in case of delayed ovulation due to LH-deficiency
- Induction/synchronization of ovulation within the framework of systems for timed inseminations
- Stimulation of the ovaries during the puerperal period from day 12 post partum
- Ovarian cysts (due to LH-deficiency)

Pigs (sows, gilts):

- Induction/synchronization of ovulation within the framework of systems for timed insemination and parturition synchronization

Horses (mares):

- Acycilia and anoestrus due to LH-deficiency

4.3 Contraindications

Do not use in cows with a mature tertiary follicle ready to ovulate.

Do not use during infectious diseases and other relevant health disorders.

Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

To maximise conception rates of cows to be treated with GnRH-PGF_{2α} based synchronization protocols, the ovarian status should be determined and regular cyclic ovarian activity confirmed. Optimal results will be achieved in healthy normally cycling cows.

4.5 Special precautions for use

Special precautions for use in animals

None.

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

Administration should be performed with caution in order to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. As GnRH analogues can be absorbed through the skin, accidental spillage onto skin or into the eyes should be thoroughly rinsed off with water. The veterinary medicinal product should not be administered by pregnant women. Women of child-bearing potential should administer the product with caution. People with known hypersensitivity to GnRH should avoid contact with the veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Pregnancy:

Not applicable.

Lactation:

Can be used during lactation.

4.8 Interaction with other medicinal products and other forms of interaction

A synergistic effect occurs in case of combined administration with FSH, especially in case of a disturbed puerperal course. Simultaneous use of human or equine chorionic gonadotropin may lead to ovarian over-stimulation.

4.9 Amounts to be administered and administration route

For intramuscular or subcutaneous injection. For intramuscular use, preferably in the neck region. The product is intended for single administration except when used as part of the “Ovsynch” timed artificial insemination protocol. Dosage in ml product and micrograms Gonadorelin[6-D-Phe] per animal.

<u>Cattle (cows and heifers)</u> by intramuscular injection: (corresponding to 50 – 100 micrograms of Gonadorelin[6-D-Phe])	1.0 - 2.0 ml
- Ovulation induction in case of delayed ovulation due to LH-deficiency	2.0 ml
- Induction/synchronization of ovulation within the framework of systems for timed inseminations	1.0 - 2.0 ml
- Stimulation of the ovaries during the puerperal period from day 12 post partum	1.0 ml
- Ovarian cysts (due to LH-deficiency)	2.0 ml

<u>Pigs (sows and gilts)</u> by intramuscular or subcutaneous injection: (corresponding to 25 – 75 micrograms of Gonadorelin[6-D-Phe])	0.5 - 1.5 ml
- Induction/synchronization of ovulation within the framework of systems for timed inseminations and parturition synchronization	

Sows: 0.5 - 1.0 ml

Gilts: 1.0 - 1.5 ml

Horses (mares) by intramuscular injection:
(corresponding to 100 micrograms of Gonadorelin[6-D-Phe])

2.0 ml

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 20 ml and 50 ml vials to avoid excessive puncturing of the closure.

Special information

Cattle:

For oestrus and ovulation synchronization and timed artificial insemination (AI) in cattle the so called “Ovsynch-procedure” was developed, which consists of the combined use of GnRH and PGF_{2α}. The following timed AI protocol has been commonly reported in the literature:

Day 0:	Inject 100 micrograms of Gonadorelin[6-D-Phe] per animal (2 ml of the product)
Day 7:	Inject PGF _{2α} or analogue (luteolytic dose)
Day 9:	Inject 100 micrograms of Gonadorelin[6-D-Phe] per animal (2 ml of the product)
AI:	16 – 20 hours later, or at observed oestrus if sooner

The Ovsynch-procedure may not be as efficacious in heifers as in cows.

Pigs:

The ovulation synchronization system includes the administration of Peforelin or PMSG after the end of oestrus synchronisation with Altrenogest in gilts or after the weaning in adult sows and two timed artificial inseminations. In adult sows the time table depends on the duration of the suckling period. The following procedures are recommended:

	Gilts*	Adult sows**
Induction of oestrus	Peforelin 48 h or PMSG (eCG) 24 h - 48 h after last application of Altrenogest	Peforelin or PMSG application 24 h after weaning
Synchronization of ovulation	Gonadorelin[6-D-Phe] 78 - 80 h after Peforelin or PMSG application	<i>Suckling period > 4 weeks:</i> Gonadorelin[6-D-Phe] 56 - 58 h after Peforelin or PMSG application <i>Suckling period 4 weeks:</i> Gonadorelin[6-D-Phe] 72 h after Peforelin or PMSG application <i>Suckling period 3 weeks:</i> Gonadorelin[6-D-Phe] 78 - 80 h after Peforelin or PMSG application
1 st AI	24 - 26 h after Gonadorelin[6-D-Phe] application	24 - 26 h after Gonadorelin[6-D-Phe] application
2 nd AI	40 - 42 h after Gonadorelin[6-D-Phe] application	40 - 42 h after Gonadorelin[6-D-Phe] application

* The preferred dose of Gonavet Veyx in gilts is 50 micrograms Gonadorelin[6-D-Phe]. However, the dose may be adjusted within the range of 50 - 75 micrograms to take into account farm-specific aspects or seasonal influences. The proposed time table should be strictly kept.

** The preferred dose of Gonavet Veyx in adult sows is 50 micrograms Gonadorelin[6-D-Phe]. However, the administration of 25 micrograms is also sufficient in case of sows with sow parity of more than 3 or during the mating period of September until May. The proposed time table should be strictly kept.

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

None known.

4.11 Withdrawal period(s)

Cattle, pigs, horses	Meat and offal:	Zero days
Cattle, horses	Milk:	Zero hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Systemic hormonal preparations, excl. sex hormone and insulin.

ATCvet code: QH01CA01 (Gonadorelin)

5.1 Pharmacodynamic properties

Gonadorelin[6-D-Phe] is an agonist of the natural gonadotropin releasing hormone (GnRH) formed in the hypothalamus that is excreted in a pulsatile manner into the pituitary portal vein circulation and controls the synthesis of the follicle stimulating hormone (FSH) and luteinising hormone (LH) in the gonadotropic cells of the anterior pituitary gland as well as LH secretion. The pulse frequency and amplitude of the GnRH excretion are dependent on the stage of the cycle. Along with FSH, LH stimulates the release of estrogens from maturing follicles in the ovaries and induces ovulation in the female organism.

Gonadorelin[6-D-Phe] acetate has the same effect as endogenous GnRH: the LH peak in the spontaneous cycle is imitated and causes follicular maturation and ovulation or stimulates a new follicle maturation wave.

With high dosage repeated or continuous application of an agonist, the gonadotropic cells in the pituitary become temporarily refractory.

5.2 Pharmacokinetic particulars

Following parenteral administration, GnRH and its analogues are absorbed rapidly and are distributed and eliminated from the organism following one-compartment-model kinetics. The plasma half-life is a few minutes (natural GnRH) up to 2 hours. The biological half-life of the natural, as well as the synthetic agonists, is short. Break-down occurs by enzymes in the form of peptidases and the excretion is primarily renal. The degradation products have no hormonal activity.

Gonadorelin[6-D-Phe] is a linear decapeptide that can only be differentiated using the difference in the amino acid at position 6 of GnRH: instead of glycine in GnRH the agonist contains D-phenylalanine. This modification leads to a higher resistance against the catabolising enzymes.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol
Sodium hydroxide (for pH adjustment)
Acetic acid, glacial (for pH adjustment)
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:

2 years

Shelf life after first opening of the immediate packaging:

28 days

6.4. Special precautions for storage

Store in a refrigerator (2 °C - 8 °C). Keep the vial in the outer carton in order to protect from light.

Do not store above 25 °C after opening.

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

<Date of first authorisation:> <{DD/MM/YYYY}><{DD month YYYY}>.>

<Date of last renewal:> <{DD/MM/YYYY}> <{DD month YYYY}>.>

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**Cardboard box for 10 ml / 20 ml / 50 ml vial****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Gonavet Veyx 50 µg/ml solution for injection
Gonavet Veyx 50 micrograms/ml solution for injection (IE/UK/EE)
Gonavet Veyx Depherelin 50 micrograms/ml solution for injection (PL)
Gonadorelin[6-D-Phe]

2. STATEMENT OF ACTIVE SUBSTANCES

Gonadorelin[6-D-Phe] 50 micrograms/ml (equivalent to 52.4 micrograms/ml Gonadorelin[6-D-Phe] acetate)

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

10 ml
20 ml
50 ml

5. TARGET SPECIES

Cattle (cows, heifers), pigs (sows, gilts), horses (mares)

6. INDICATION(S)**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

For intramuscular and subcutaneous use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period:
Cattle, pigs, horses Meat and offal: Zero days
Cattle, horses Milk: Zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Pregnant women should not handle this product.
Read the package leaflet before use.

10. EXPIRY DATE

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

11. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Keep the vial in the outer carton in order to protect from light.
Do not store above 25 °C after opening.

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

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 / 20 ml / 50 ml vials****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Gonavet Veyx 50 µg/ml solution for injection for cattle, pigs and horses

Gonavet Veyx 50 micrograms/ml solution for injection for cattle, pigs and horses (IE/UK/EE)

Gonavet Veyx Depherelin 50 micrograms/ml solution for injection for cattle, pigs and horses (PL)

Gonadorelin[6-D-Phe]

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

50 micrograms/ml

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

10 ml

20 ml

50 ml

4. ROUTE(S) OF ADMINISTRATION

IM, SC

5. WITHDRAWAL PERIOD(S)

Withdrawal period:

Cattle, pigs, horses

Meat and offal:

Zero days

Cattle, horses

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.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

Gonavet Veyx 50 µg/ml solution for injection for cattle, pigs and horses (DE, AT, BE, BG, CZ, EL, ES, FR, HU, HR, IS, IT, LT, LU, LV, NL, PT, RO, SI, SK)

Gonavet Veyx 50 micrograms/ml solution for injection for cattle, pigs and horses (IE/UK/EE)

Gonavet Veyx Depherelin 50 micrograms/ml solution for injection for cattle, pigs and horses (PL)

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

Marketing authorization holder and manufacturer responsible for batch release:

Veyx-Pharma GmbH
Söhreweg 6
34639 Schwarzenborn
Germany

Manufacturer responsible for batch release:

Veyx Pharma BV
Forellenweg 16
NL-4941 SJ Raamsdonksveer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gonavet Veyx 50 µg/ml solution for injection for cattle, pigs and horses
Gonadorelin[6-D-Phe]

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

Gonavet Veyx is a clear colourless solution for injection containing:

Active substance:

Gonadorelin[6-D-Phe] 50 micrograms/ml (equivalent to 52.4 micrograms/ml Gonadorelin[6-D-Phe] acetate)

Excipients:

Chlorocresol 1 mg/ml

4. INDICATION(S)

Control and stimulation of reproduction in cattle and pigs. Treatment of ovarian-related fertility disorders or dysfunctions in cattle and horses.

Cattle (cows, heifers):

- Ovulation induction in case of delayed ovulation due to LH-deficiency
- Induction/synchronization of ovulation within the framework of systems for timed inseminations
- Stimulation of the ovaries during the puerperal period from day 12 post partum
- Ovarian cysts (due to LH-deficiency)

Pigs (sows, gilts):

- Induction/synchronization of ovulation within the framework of systems for timed insemination and parturition synchronization

Horses (mares):

- Acycilia and anoestrus due to LH-deficiency

5. CONTRAINDICATIONS

Do not use in cows with a mature tertiary follicle ready to ovulate.
Do not use during infectious diseases and other relevant health disorders.
Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

None known.

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.
Alternatively, you can report via your national reporting system {national system details}.

7. TARGET SPECIES

Cattle (cows, heifers), pigs (sows, gilts), horses (mares)

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

For intramuscular or subcutaneous injection. For intramuscular use, preferably in the neck region. The product is intended for single administration except when used as part of the “Ovsynch” timed artificial insemination protocol. Dosage in ml product and micrograms Gonadorelin[6-D-Phe] per animal.

<u>Cattle (cows and heifers)</u> by intramuscular injection:	1.0 - 2.0 ml
(corresponding to 50 – 100 micrograms of Gonadorelin[6-D-Phe])	
- Ovulation induction in case of delayed ovulation due to LH-deficiency	2.0 ml
- Induction/synchronization of ovulation within the framework of systems for timed inseminations	1.0 - 2.0 ml
- Stimulation of the ovaries during the puerperal period from day 12 post partum	1.0 ml
- Ovarian cysts (due to LH-deficiency)	2.0 ml
<u>Pigs (sows and gilts)</u> by intramuscular or subcutaneous injection:	0.5 - 1.5 ml
(corresponding to 25 – 75 micrograms of Gonadorelin[6-D-Phe])	
- Induction/synchronization of ovulation within the framework of systems for timed inseminations and parturition synchronization	
Sows:	0.5 - 1.0 ml
Gilts:	1.0 - 1.5 ml
<u>Horses (mares)</u> by intramuscular injection:	2.0 ml
(corresponding to 100 micrograms of Gonadorelin[6-D-Phe])	

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 20 ml and 50 ml vials to avoid excessive puncturing of the closure.

Special information

Cattle:

For oestrus and ovulation synchronization and timed artificial insemination (AI) in cattle the so called “Ovsynch-procedure” was developed, which consists of the combined use of GnRH and PGF_{2α}. The following timed AI protocol has been commonly reported in the literature:

Day 0:	Inject 100 micrograms of Gonadorelin[6-D-Phe] per animal (2 ml of the product)
Day 7:	Inject PGF _{2α} or analogue (luteolytic dose)
Day 9:	Inject 100 micrograms of Gonadorelin[6-D-Phe] per animal (2 ml of the product)
AI:	16 – 20 hours later, or at observed oestrus if sooner

The Ovsynch-procedure may not be as efficacious in heifers as in cows.

Pigs:

The ovulation synchronization system includes the administration of Peforelin or PMSG after the end of oestrus synchronisation with Altrenogest in gilts or after the weaning in adult sows and two timed artificial inseminations. In adult sows the time table depends on the duration of the suckling period. The following procedures are recommended:

	Gilts*	Adult sows**
Induction of oestrus	Peforelin 48 h or PMSG (eCG) 24 h - 48 h after last application of Altrenogest	Peforelin or PMSG application 24 h after weaning
Synchronization of ovulation	Gonadorelin[6-D-Phe] 78 - 80 h after Peforelin or PMSG application	<i>Suckling period > 4 weeks:</i> Gonadorelin[6-D-Phe] 56 - 58 h after Peforelin or PMSG application <i>Suckling period 4 weeks:</i> Gonadorelin[6-D-Phe] 72 h after Peforelin or PMSG application <i>Suckling period 3 weeks:</i> Gonadorelin[6-D-Phe] 78 - 80 h after Peforelin or PMSG application
1 st AI	24 - 26 h after Gonadorelin[6-D-Phe] application	24 - 26 h after Gonadorelin[6-D-Phe] application
2 nd AI	40 - 42 h after Gonadorelin[6-D-Phe] application	40 - 42 h after Gonadorelin[6-D-Phe] application

* The preferred dose of Gonavet Veyx in gilts is 50 micrograms Gonadorelin[6-D-Phe]. However, the dose may be adjusted within the range of 50 - 75 micrograms to take into account farm-specific aspects or seasonal influences. The proposed time table should be strictly kept.

** The preferred dose of Gonavet Veyx in adult sows is 50 micrograms Gonadorelin[6-D-Phe]. However, the administration of 25 micrograms is also sufficient in case of sows with sow parity of more than 3 or during the mating period of September until May. The proposed time table should be strictly kept.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIOD(S)

Cattle, pigs, horses	Meat and offal:	Zero days
Cattle, horses	Milk:	Zero hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store in a refrigerator (2 °C – 8 °C). Keep the vial in the outer carton in order to protect from light.

Do not store above 25 °C after opening.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and vial label after “EXP”. The expiry date refers to the last day of that month. Shelf life after first opening the immediate packaging: 28 days.

When the container is broached (opened) for the first time, the date on which any product remaining in the vial should be discarded should be worked out by using the in-use shelf life which is specified on this package insert. This discard date should be written in the space provided on the label.

12. SPECIAL WARNING(S)

Special warnings for each target species:

To maximise conception rates of cows to be treated with GnRH-PGF_{2α} based synchronization protocols, the ovarian status should be determined and regular cyclic ovarian activity confirmed. Optimal results will be achieved in healthy normally cycling cows.

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

Administration should be performed with caution in order to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. As GnRH analogues can be absorbed through the skin, accidental spillage onto skin or into the eyes should be thoroughly rinsed off with water. The veterinary medicinal product should not be administered by pregnant women. Women of child-bearing potential should administer the product with caution. People with known hypersensitivity to GnRH should avoid contact with the veterinary medicinal product.

Lactation:

Can be used during lactation.

Interaction with other medicinal products and other forms of interaction:

A synergistic effect occurs in case of a combined administration with FSH, especially in case of a disturbed puerperal course. Simultaneous use of human or equine chorionic gonadotropin may lead to an ovarian over-stimulation.

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

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.