[Version 9,03/2022]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

INDUPART 75 micrograms /mL solution for injection for cattle, pigs and horses [**AT / BG / CZ / DE / ES / HU / LT / LV / PT / SK / RO / BE / IE / LU / NL]**

INDUPART [**DK]**

GANAPAR 75 micrograms /mL solution for injection for cattle, pigs and horses **[PL / EE]**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
75 µg of D-cloprostenol as D-cloprostenol sodium

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Chlorocresol	1.0 mg
Ethanol 96%	
Sodium hydroxide (for pH adjustment)	
Citric acid anhydrous (for pH adjustment)	
Water for injections	

Solution for injection. Clear colourless solution

3. CLINICAL INFORMATION

3.1 Target species

Cattle (cows), pigs (sows) and horses (mares).

3.2 Indications for use for each target species

Cattle:

- Synchronisation or induction of oestrus
- Induction of parturition;
- Ovarian dysfunction (persistent *corpus luteum*, luteal cyst);
- Endometritis/pyometra;
- Delayed uterine involution;
- Induction of abortion in the first half of pregnancy
- Expulsion of mummified foetuses;

Pigs:
Induction of parturition.

Horses:
Induction of luteolysis in mares with a functional *corpus luteum.*

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in pregnant animals, unless it is desirable to induce parturition or induction of abortion.
Do not administer intravenously.
Do not use in animals with cardiovascular, gastro-intestinal or respiratory problems.
Do not administer to induce parturition in sows and cows with suspected dystocia due to mechanical obstruction or if problems are expected because of an abnormal position of the foetus.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Induction of parturition and abortion may increase the risk of complications, retained placenta, foetal death and metritis.
To reduce the risk of anaerobic infections, which might be related to the pharmacological properties of prostaglandins, care should be taken to avoid injection through contaminated areas of skin. Clean and disinfect injection sites thoroughly before administration.
In case of oestrus induction in cows: from the 2nd day after injection, adequate heat detection is necessary.
Induction of parturition in sows before day 114 of gestation may result in an increased risk of stillbirths and the need for manual assistance at farrowing.

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

d-Cloprostenol, like all $F_{2\alpha}$ prostaglandins, can be absorbed through the skin and can produce bronchospasm and abortion.
Direct contact with skin or mucous membranes of the user should be avoided. Pregnant women, women of child-bearing age, asthmatics and persons with bronchial problems or any other type of respiratory problem must avoid any contact or use disposable plastic gloves when administering the veterinary medicinal product.

The veterinary medicinal product must be handled carefully to avoid accidental self-injection or skin contact.
In case of accidental self injection seek medical advice immediately and show the package leaflet or the label to the physician.
Seek medical advice immediately in case of any respiratory difficulty caused by accidental inhalation or inoculation.
In case of accidental skin contact, wash with soap and water immediately.
Do not eat, drink or smoke while handling the veterinary medicinal product.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cows:

Undetermined frequency (cannot be estimated from the available data):	Injection site infection (injection site swelling, crepitus)[1] Retained placenta [2]

1. If anaerobic bacteria penetrate the tissue of the injection site.
2. The incidence may be increased when used in cows for induction parturition and dependent on the time of treatment relative to the date of conception.

Sows:

Undetermined frequency (cannot be estimated from the available data):	Behavioural changes[1]

1. Similar to those changes associated with natural farrowing and usually cease within one hour.

Horses:
None known

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:
Do not use (during the whole or part of the pregnancy) unless it is desirable to induce parturition or therapeutic interruption of pregnancy, as the use in gestating animals produces abortion.

3.8 Interaction with other medicinal products and other forms of interaction

Do not administer the veterinary medicinal product together with non-steroidal anti-inflammatory drugs since they inhibit endogenous prostaglandin synthesis.
The activity of other oxytocic agents can be increased after the administration of cloprostenol.

3.9 Administration routes and dosage

Intramuscular use.

Cows: Administer 2 ml of the veterinary medicinal product/animal, equivalent to 150 µg of d-cloprostenol/animal:

- Synchronisation of oestrus: administer the veterinary medicinal product twice, with an interval of 11 days between each dose. Proceed therefore with two artificial inseminations at intervals of 72 and 96 hours from the second injection.

- Induction of oestrus (also in cows showing weak or silent heat): administer veterinary medicinal product after having established the presence of a corpus luteum (6-18th day of the cycle); heat usually appears within 48-60 hours. Proceed, therefore, with insemination 72-96 hours after injection. If oestrus is not evident, administration of the veterinary medicinal product needs to be repeated 11 days after the first injection.
- Induction of parturition after day 270 of gestation: administer the veterinary medicinal product after 270 days of pregnancy. Parturition usually results within 30-60 hours of treatment.
- Ovarian dysfunction(persistent *corpus luteum*, luteal cyst): when the presence of the corpus luteum is determined administer the veterinary medicinal product, then proceed to inseminate at the first oestrus after injection. If oestrus is not evident, conduct a further gynaecological examination, and repeat the injection 11 days after the first administration. Insemination must always be carried out 72-96 hours after injection.
- Endometritis, pyometra: administer 1 dose of the veterinary medicinal product. If necessary repeat the treatment after 10days.
- Induction of abortion in the first half of pregnancy (until day 150 of pregnancy): administer veterinary medicinal product in the first half of pregnancy.
- Expulsion of mummified foetus: administer 1 dose of the veterinary medicinal product. Expulsion of the foetus is observed within 3-4 days after administration of the veterinary medicinal product.
- Delayed uterine involution: administer veterinary medicinal product and, if considered necessary, carry out one or two successive treatments at 24 hour intervals.

Sows: Administer 1 ml of the veterinary medicinal product/animal equivalent to 75 micrograms of d-cloprostenol/animal, by intramuscular route, not earlier than 114 days of pregnancy. Repeat after 6 hours. Alternatively, 20 hours after the initial dose, a myometrial stimulant (oxytocin or carazolol) may be administered.
Following the protocol of the double administration, approximately 70-80% of the animals will give birth during the interval between 20 and 30 hours after the first administration.

Mares: Induction of luteolysis in mares with a functional *corpus luteum:* Administer 1 ml of the veterinary medicinal product/animal, equivalent to 75 µg of d-cloprostenol/animal.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

At 10 times the therapeutic dose, no adverse reactions were reported in cows and sows. In general, a large overdose could result in the following symptoms: increased pulse and breathing rate, bronchoconstriction, increased body temperature, increased amounts of loose faeces and urine, salivation and vomiting. As no specific antidote has been identified, in the case of overdose, symptomatic therapy is advisable. An overdose will not accelerate corpus luteum regression.

In mares, moderate sweating and soft faeces was detected when administered 3 times the therapeutic dose.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.
[ES]: Administration under the control or direct responsibility of a veterinary surgeon.

3.12 Withdrawal periods

Cattle: Meat and offal: Zero days
Milk: Zero hours

Pigs: Meat and offal: 1 day

Horses: Meat and offal: 2 days
Milk: Zero hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QG02AD90

4.2 Pharmacodynamics

The veterinary medicinal product contains dextrorotatory cloprostenol (d-cloprostenol), a synthetic analogue of the prostaglandin $F_{2\alpha}$. D-cloprostenol is the biologically active luteal component of the cloprostenol.
The veterinary medicinal product is approximate 3.5 times more potent than similar specialities of racemic cloprostenol. For this reason, it could be used in a proportionally lower dose level.
The veterinary medicinal product is more effective and better tolerated than racemic cloprostenol.
Administered in the luteal phase of the oestrus cycle, D-cloprostenol induces a diminution of the number of the luteinizing hormone (LH) receptors in the ovary, this induces a functional and morphological regression of the corpus luteum (luteolysis) resulting in a sharp fall in progesterone levels. The anterior part of the pituitary gland increases the release of the follicle stimulating hormone (FSH), this induces the follicular maturation followed by signs of oestrus and by ovulation.

4.3 Pharmacokinetics

After intramuscular administration of 75 µg of d-cloprostenol to sows, the maximum concentration of d-cloprostenol in plasma was close to 2 µg/l and occurred between 30 and 80 minutes after injection. The half-life of elimination $T_{1/2\beta}$ was estimated to be 3 h 10 min.
In cows, after intramuscular administration of 150 µg of d-cloprostenol/cow, the highest plasma concentration of d-cloprostenol was found at 90 minutes after injection (approximately 1.4 µg/l).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

Keep the vial in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

The veterinary medicinal product is packaged in type I colourless glass vials closed with bromobutyl rubber stopper and sealed with aluminum cap.
Pack sizes:
Carton box with 1 vial of 20 ml.
Carton box with 5 vials of 20 ml.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

VETPHARMA ANIMAL HEALTH, S.L.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

DD month YYYY

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).