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:
D-Cloprostenol (as D-cloprostenol sodium) 75µg

Excipients:
Chlorocresol ..... 1.0 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), pigs (sows) and horses (mares)

4.2 Indications for use, specifying the 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.*

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in pregnant females, 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.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

- 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

Prostaglandins of the $F_{2\alpha}$ type can be absorbed through the skin and may cause bronchospasm or miscarriage.
Care should be taken when handling the product to avoid self-injection or skin contact.
Women of child-bearing age, asthmatics and people with bronchial or other respiratory problems, should avoid contact with, or wear disposable impervious gloves when administering 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 shortness of breath result from accidental inhalation or injection, seek medical advice immediately and show the package leaflet or label to the physician.
Do not eat, drink or smoke while handling the product.

4.6 Adverse reactions (frequency and seriousness)

Occurrence of bacterial infection is likely if anaerobic bacteria penetrate the tissue of the injection site. This applies in particular to cows.

Typical local reactions due to anaerobic infection are swelling and crepitus at the injection site.

When used in cows for induction of parturition and dependent on the time of treatment relative to the date of conception, the incidence of retained placenta may be increased.

Behavioural changes in sows seen after treatment for induction of farrowing are similar to those changes associated with natural farrowing and usually cease within 1 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

The use in gestating animals produces abortion.

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer the 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.

4.9 Amounts to be administered and administration route

Only for intramuscular use.

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

- Synchronisation of oestrus: administer the 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 product needs to be repeated 11 days after the first injection.
- Induction of parturition after day 270 of gestation: administer the 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 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 product in the first half of pregnancy.
- Expulsion of mummified foetus: administer 1 dose of the product. Expulsion of the foetus is observed within 3-4 days after administration of the 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.

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

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.

4.11 Withdrawal period(s)

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

Pigs: Meat and offal: 1 day

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

5. PHARMACOLOGICALPROPERTIES

Pharmacotherapeutic group: prostaglandins.
ATC vet code: QG02AD90

5.1 Pharmacodynamic properties

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 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.

5.2 Pharmacokinetic particulars

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).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol
Ethanol 96%
Sodium hydroxide (for pH adjustment)
Citric acid anhydrous (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 the immediate packaging: 28 days

6.4. Special precautions for storage

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

6.5 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.

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

VETPHARMA ANIMAL HEALTH, S.L.
Les Corts, 23
08028 Barcelona
Spain

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23/04/2014
Date of last renewal:

10 DATE OF REVISION OF THE TEXT

DD month YYYY

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription.