

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box with 1 vial of 20 ml
Box with 5 vials of 20 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prellim 0.075 mg/ml solution for injection.

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:

Active substance:

d-Cloprostenol (as d-Cloprostenol sodium) 0.075 mg

Excipient:

Chlorocresol1 mg

3. PACKAGE SIZE

20 ml

5 x 20 ml

4. TARGET SPECIES

Cattle (cows) and pigs (sows).

5. INDICATION(S)

6. ROUTE(S) OF ADMINISTRATION

Intramuscular use.

7. WITHDRAWAL PERIODS

Cows: Meat and offal: 1 day.

Milk: Zero hours.

Sows: Meat and offal: 1 day.

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened, used within 28 days.
Once opened used by ...

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”.

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Laboratorios Syva S.A.
Calle Marqués de la Ensenada 16
28004 Madrid
Spain

14. MARKETING AUTHORISATION NUMBER(S)

Vm 31592/5003

15. BATCH NUMBER

Lot {number}

16. SPECIAL WARNING(S), IF NECESSARY

17. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read package leaflet.

18. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IF APPLICABLE

POM-V ('To be supplied only on veterinary prescription')

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGE UNITS
Vial of 20 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prellim 0.075 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE

Each ml contains:

d-Cloprostenol (as d-Cloprostenol sodium) 0.075 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {month/year}

Once opened, used within 28 days.

Once opened used by...

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

20 ml

6. ROUTE(S) OF ADMINISTRATION

Intramuscular use.

7. WITHDRAWAL PERIOD

Cows: Meat and offal: 1 day.

Milk: Zero hours.

Sows: Meat and offal: 1 day.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PARTICULARS TO APPEAR ON THE PACKAGE LEAFLET:

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prellim 0.075 mg/ml solution for injection for cattle and pigs

2. COMPOSITION

Each ml contains:

Active substance:

d-Cloprostenol (as d-Cloprostenol sodium).....0.075 mg

Excipients:

Chlorocresol1 mg

Clear, colourless solution for injection, free from particles in suspension.

3. TARGET SPECIES

Cattle (cows) and Pigs (sows).

4. INDICATIONS FOR USE

Cattle (cows)

Indications for reproduction: synchronization or induction of oestrus. Induction of parturition.

Therapeutic indication: ovarian dysfunction (persistent corpus luteum, luteal cyst), interruption of gestation including foetal mummification, endometritis/pyometra, delayed uterine involution.

Pigs (sows)

Indications for reproduction: Induction of parturition.

5. CONTRAINDICATIONS

Do not use (during the whole or part of the pregnancy) unless it is desirable to induce parturition or therapeutic interruption of pregnancy. Do not use in case of hypersensitivity to the active substance, or to any of the excipients. Do not use in animal with spastic respiratory or gastro-intestinal diseases.

6. SPECIAL WARNING(S)

Special warnings:

None

Special precautions for safe use in the target species:

As with parenteral administration of any substance, basic antiseptic rules should be observed. The injection site must be thoroughly cleaned and disinfected in order to reduce the risk of infection with anaerobic bacteria.

Pigs: use only when precise date of insemination is known. Administer on day 113 of gestation, at the earliest. The veterinary medicinal product administered earlier, may impair the viability and weight of piglets.

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

d-Cloprostenol, like all F₂ α 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

Pregnancy:

Do not use (during the whole or part of the pregnancy) unless it is desirable to induce parturition or therapeutic interruption of pregnancy.

Interaction with other medicinal products and other forms of interaction:

Do not use in animals being treated with non-steroidal anti-inflammatories, as the synthesis of endogenous prostaglandins is inhibited.

The activity of other oxytocic agents can be increased after the administration of Cloprostenol.

Overdose:

In safety studies, at 10 times the therapeutic dose, no adverse reactions are reported.

As no specific antidote has been identified, in the case of overdose, symptomatic therapy is advisable.

Special restrictions for use and special conditions for use:

Administration by a veterinarian surgeon or under their close supervision.

Major incompatibilities:

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

7. ADVERSE EVENTS

Cattle and pigs

Very rare

(< 1 animal/ 10,000 animals treated, including isolated reports):

Application site reaction¹

Injection site swelling¹

Injection site gaseous gangrene¹

¹Typical local reactions due to anaerobic infection applies in particular to cows.

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system Website: <https://www.gov.uk/report-veterinary-medicine-problem/animal-reacts-medicine> e-mail: adverse.events@vmd.gov.uk

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

This veterinary medicinal product is only for intramuscular use:

Cattle (cows): The recommended dose is 0.150 mg d-cloprostenol/animal, equivalent to 2 ml/animal.

- **Oestrus induction** (also in cows with weak or silent heat): Administer the veterinary medicinal product after the presence of corpus luteum has been determined (6th-18th day of the cycle). Heat is normally observed after 48-60 hours. Inseminate 72-96 hours after the previous treatment.

If heat is not observed, repeat after 11 days.

- **Parturition induction:** Administer the veterinary medicinal product after the 270th day of gestation. Parturition should occur 30-60 hours after treatment.

- **Oestrus synchronization:** Administer the veterinary medicinal product twice (11 days apart). Inseminate artificially 72 and 96 hours after the second injection.

Based on the results of clinical trials and the scientific literature, d-cloprostenol can be used in combination with GnRH, with or without progesterone, in ovulation synchronization protocols (Ovsynch protocols). The decision on which protocol to use should be made by the responsible veterinarian, based on the objectives of the treatment and depending on the herd and animals to be treated. The following protocols have been evaluated and can be used:

In cyclical cows:

- Day 0: inject GnRH (or analog).

- Day 7: inject d-cloprostenol (2 ml of the veterinary medicinal product).
- Day 9: inject GnRH (or analog).
- Artificial insemination 16-24 hours later.

Alternatively in cyclical and non-cyclical cows and heifers:

- Day 0: insert the intravaginal progesterone releasing device and inject GnRH (or analog).
 - Day 7: remove the intravaginal device and inject d-cloprostenol (2 ml of the veterinary medicinal product).
 - Day 9: inject GnRH (or analog).
 - Artificial insemination 16-24 hours later.
- **Ovarian dysfunction:** After the presence of corpus luteum has been determined, administer the veterinary medicinal product and inseminate during the first heat after treatment. If no heat is observed, carry out another gynaecological examination and repeat the injection 11 days after the first treatment. Inseminate 72-96 hours after treatment.
 - **Endometritis or pyometra:** Administer 1 dose of veterinary medicinal product. Repeat treatment 10-11 days later if necessary.
 - **Gestation interruption:** Administer the veterinary medicinal product during the first half of gestation.
 - **Foetal mummification:** Administer 1 dose of veterinary medicinal product. The foetus is expelled 3 or 4 days later.
- **Retarded uterine involution:** Administer 1 dose of veterinary medicinal product and, if indicated, repeat treatment once or twice at 24 hours interval.

Pigs (sows): The recommended dose is 0.075 mg d-cloprostenol/animal, equivalent to 1 ml/animal.

- **Parturition induction:** Administer the veterinary medicinal product after day 112 of gestation. Repeat after 6 hours. Alternatively, 20 hours after the initial dose of d-cloprostenol, a myometrial stimulant (oxytocin or carazolol) may be administered. Following the protocol of double administration, in about 70% of cases, parturition occurs 20-30 hours after the first treatment.

9. ADVICE ON CORRECT ADMINISTRATION

As with parenteral administration of any substance, basic antiseptic rules should be observed. The injection site must be thoroughly cleaned and disinfected in order to reduce the risk of infection with anaerobic bacteria.

10. WITHDRAWAL PERIOD

Cows:

Meat and offal: 1 day.

Milk: Zero hours.

Sows:

Meat and offal: 1 day.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Keep the vial in the outer carton in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 28 days.

When the container is broached for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be determined. This discard date should be written in the space provided.

12. SPECIAL PRECAUTIONS FOR DISPOSAL

Medicines should not be disposed of via wastewater.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

Ask your veterinary surgeon *or pharmacist* how to dispose of medicines no longer required. These measures should help to protect the environment.

13. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Veterinary medicinal product subject to prescription.

14. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Vm 31592/5003

Package sizes:

1 glass vial of 20 ml in a cardboard box.
5 glass vials of 20 ml in a cardboard box.

Not all pack sizes may be marketed.

15. **PID LINK (Do not print heading)**

[The following statement must be included where reference to the European Union Product Database is included on the product information. This statement is relevant to both UK(GB) and UK(NI) products:]

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

16. CONTACT DETAILS

Marketing authorisation holder:

Laboratorios Syva S.A.
Calle Marqués de la Ensenada 16
28004 Madrid
Spain

Manufacturer responsible for batch release:

Laboratorios Syva S.A.
Avenida Párroco Pablo Díez, 49-57
San Andrés del Rabanedo
24010 León
Spain

Local representative:

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey, KT22 7LP
UK
Tel: + 44 (0) 845 300 8034

Contact details to report suspected adverse reactions:

Zoetis UK Limited
Tel: + 44 (0) 845 300 8034

17. OTHER INFORMATION

Gavin Hall

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