B. PACKAGE LEAFLET

PACKAGE LEAFLET:

1. Name of the veterinary medicinal product

Synchromate 0.25 mg/ml, Solution for injection for cattle, pigs and horses

2. Composition

Each ml of solution contains:
Active substance:
Cloprostenol 0.25 mg
(corresponds to Cloprostenol sodium 0.263 mg)

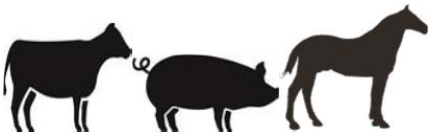
Excipients:

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
Citric acid monohydrate	-
Ethanol (96 per cent)	-
Sodium chloride	-
Sodium citrate	-
Water for injections	-

Clear colorless solution.

3. Target species

Cattle, pigs and horses



4. Indications for use

Cattle (Cows):
- Subestrous or silent oestrus
- Treatment of luteal cysts.
- Induction and synchronization of estrus

- Termination of pregnancy until day 150 of pregnancy
- Expulsion of mummified foetus
- Induction of parturition after 270 days of pregnancy
- Adjuvant treatment in chronic endometritis and pyometra.

Pigs (Sows):
- Induction of labor or synchronization of labor from day 114 of pregnancy (the last insemination day counted as the 1st day of pregnancy).

Horses (Mares):
- Induction of luteolysis.
- Treatment of persistent dioestrus.
- Treatment of pseudo-pregnancy.
- Treatment of lactation anestrus.
- Induction of estrous cycle.
- Induction of labour after 320 days of pregnancy.

5. Contraindications

- Do not administer to pregnant animals in which induction of abortion or parturition is not desired.
- Do not administer in case of spastic disease of the respiratory system and gastrointestinal tract and cardiovascular diseases.
- Do not use to induce abortion in case of dystocia due to mechanical obstruction or abnormal positioning of foetus.
- Do not use in case of known hypersensitivity to active substance or excipients.
- Do not administer intravenously

6. Special warnings

Avoid induction of too early farrowing in multiparous and primiparous sows.
Induction of labour two days prior to the average duration of gestation can lead to an increase in stillbirth of piglets.

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.

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

Prostaglandins of the F2α type, such as cloprostenol, 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,especially by pregnant women, women of child-bearing age, asthmatics and people with bronchial or other respiratory problems.
Wear disposable impervious gloves when administering the veterinary medicinal product.
Direct contact with the skin or eyes may cause irritation and allergic reactions.
People with known hypersensitivity to cloprostenol or chlorocresol should avoid contact with theveterinary medicinal product.
Accidental spillage on the skin or into the eyes should be washed off immediately with plenty of water.
In case of accidental self-injection or spillage on the skin, seek medical advice immediately, particularly as shortness of breath may occur, and show the package leaflet or the label to the physician.
Do not eat, drink or smoke while handling the veterinary medicinal product.

Special precautions for the protection of the environment:

Not applicable.

Pregnancy and lactation:
Do not administer to pregnant animals unless the objective is to terminate the pregnancy.
The veterinary medicinal product can be used during lactation.

Interaction with other medicinal products and other forms of interaction:
Simultaneous use of oxytocin and Cloprostenol increases the intensity and frequency of uterine contractions.

In animals treated with a progestogen, a decreased response to progestogen is to be expected.
Do not administer together with Non-steroidal Anti-inflammatory Drugs (NSAID) as they inhibit endogenous prostaglandin synthesis.

Overdose (symptoms, emergency procedures, antidotes):
In case of overdose, the following clinical signs may occur:
Increase in pulse and respiratory rate, bronchoconstriction, increase in body temperature, increased defecation and urination, salivation, nausea and vomiting.

In cattle, 200 times the dose of cloprostenol sodium caused only mild and transient scouring. In heifers, no adverse effects were noted after two intramuscular administrations, 11 days apart, of R-cloprostenol (as the sodium salt) at the recommended dose (150 µg) or at a ten-fold dose (1500 µg).

In sows, no adverse effects of R-cloprostenol (as the sodium salt) were reported after single intramuscular administration at the recommended dose (75 µg), at five-fold dose (225 µg) or at ten-fold dose (750 µg).
In horses transient clinical signs such as sweating, reduced rectal temperature, tachycardia, rapid breathing, movement incordination, colic, restlessness and depression may be observed disappearing within short time after application of the dose.

Incompatibilities:

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

7. Adverse events

Cows:

Common (1 to 10 animals / 100 animals treated):	- Retained placenta or Retained foetal membrane : (common in animals induced too early, usually more than 10 days before the calculated parturition date. Induction of parturition should take place as close as possible to the predicted calving date which is calculated based on actual conception date.)
Rare (1 to 10 animals / 10,000 animals treated):	- Injection site infection: (associated with proliferation of clostridia at the site of inoculation. Typical local reactions due to Anaerobic infection are inflammation and crepitus at the injection site. Adequate aseptic precautions are needed to avoid this adverse effect.) - Anaphylactic type reactions may be observed on rare occasions for a transient period within 15 minutes post-injection which usually disappear within an hour.
*Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Restlessness (observed within 15 minutes post-injection and usually disappear after an hour.) (Above signs may be observed within 15 minutes post-injection which usually disappear within an hour.)

Sows:

Common (1 to 10 animals / 100 animals treated):	- Retained placenta or Retained foetal membrane : - (common in animals induced too early, usually more than 10 days before the calculated parturition date. Induction of parturition should take place as close as possible to the predicted calving date which is calculated based on actual conception date.)
Rare (1 to 10 animals / 10,000 animals treated):	- Injection site infection: (associated with proliferation of clostridia at the site of inoculation. Typical local reactions due to Anaerobic infection are inflammation and crepitus at the injection site. Adequate aseptic precautions are needed to avoid this adverse effect.) Anaphylactic type reactions may be observed on rare occasions for a transient period within 15 minutes post-injection which usually disappear within an hour.
*Very rare (<1 animal / 10,000 animals treated, including isolated	- Frequent urination, - Increased bowel movements - Behavioral disorder NOS (changes in behavior similar to those that occur before farrowing, which can go on for an

reports):	hour) (Above signs may be observed within 15 minutes post-injection which usually disappear within an hour.)

Mares:

Common (1 to 10 animals / 100 animals treated):	- Retained placenta or Retained foetal membrane : - (common in animals induced too early, usually more than 10 days before the calculated parturition date. Induction of parturition should take place as close as possible to the predicted calving date which is calculated based on actual conception date.)
Rare (1 to 10 animals / 10,000 animals treated):	- Injection site infection: (associated with proliferation of clostridia at the site of inoculation. Typical local reactions due to Anaerobic infection are inflammation and crepitus at the injection site. Adequate aseptic precautions are needed to avoid this adverse effect.) Anaphylactic type reactions may be observed on rare occasions for a transient period within 15 minutes post-injection which usually disappear within an hour.
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	- Cold sweating - Colic - Prostration (Above signs may be observed within 15 minutes post-injection which usually disappear within an hour.)

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 the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

Route of application: deep intramuscular injection.

Cattle (Cows): 0.5 mg Cloprostenol/animal corresponding to 2.0 ml product / animal
Subestrus or silent heat / oestrus induction **:** Administer the drug, after determining the presence of the *corpus luteum*. Heat is generally observed within 2-5 days after treatment. Inseminate at 72-96 hours.
Pregnancy interruption **:** The administration should be carried out between the first week and the day 150 gestation. Abortion occurs after 4-5 days.
Endometritis or pyometra **:** Administer a single dose of the drug. If necessary repeat treatment 10-14 days later.

Pigs (Sows): 0.175 mg Cloprostenol/animal corresponding to 0.7 ml of product / animal as a single dose.
Induction of labor must be performed within 24-48 hours prior to the expected date of the same to reduce the risk of mortality in piglets. Delivery usually occurs at 19-29 hours of its administration.

Horses (Mares):
- **Ponies:** single dose of 0.5-1.0 ml (equivalent to 125-250 mcg of cloprostenol) per animal.
- **Thoroughbreds, hunters and heavy horses:** single dose of 1-2 ml (equivalent to 250- 500 mcg cloprostenol) per animal.

9. Advise on correct administration

To reduce the risk of anaerobic infection, thoroughly clean and disinfect the injection site before application.

For 10 ml and 20 ml vials:
The rubber stoppers of the vial may be safely punctured up to 10 times with 16-gauge needle.

For 50 ml and 100 ml vial:
The rubber stoppers of the vial may be safely punctured up to 10 times with 16-gauge needle. Otherwise, automatic syringe equipment, or a suitable draw-off needle, should be used to avoid excessive puncturing of the closure.

10. Withdrawal periods

Withdrawal period:
Cattle (cows):
Meat and offal: 2 days
Milk: Zero days
Pig (sows):
Meat and offal: 2 days

Horses (mares):
Meat and offal: 28 days.

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.

12. Special precautions for disposal

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

13. Classification of veterinary medicinal products

14. Marketing authorisation numbers and pack sizes

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

MM/YYYY

Detailed information on this veterinary medicinal product is available in the Union Product Database.

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions

Alivira Animal Health Limited
16 Glenoaks Close, Glenconner,
Clonmel, Co Tipperary
Ireland. E91T8Y6.

Manufacturer responsible for batch release:
For 10 ml, 20 ml, 50 ml and 100 ml:
Bremer Pharma GmbH
Werkstrasse 42
34414 Warburg GERMANY

Contact details to report suspected adverse reactions
Name: Teresa Vila Viña
Address: Pol. Ind. La Borda, Mas Pujades 11-
12, 08140 Caldes de Montbui, Barcelona,
Spain
Phone (24h): +34 670 620 212
Phone: +34 93865 41 48
Telefax: +34 93 865 46 48
E-mail: pharmacovigilance@karizoo.com; teresa.vila@karizoo.com

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information

Pack Sizes:

Cardboard box containing 1vial of 10ml
Cardboard box containing 5 vials of 10ml
Cardboard box containing 12 vials of 10ml
Cardboard box containing 1 vial of 20ml
Cardboard box containing 5 vials of 20ml
Cardboard box containing 12 vials of 20ml
Cardboard box containing 1 vial of 50ml
Cardboard box containing 1 vial of 100ml

Not all pack sizes may be marketed.