

CONSUMER PACKAGE INSERT FOR A VETERINARY MEDICINAL PRODUCT

The medicine is dispensed with a veterinarian's prescription only
For use in animals only

1. Name of the medicinal product and dosage form:

Estrumate Veterinary
Solution for Injection

2. Composition:

Each 1 ml comprises:

Active ingredient:

Cloprostenol sodium 0.263 mg
(equivalent to 0.250 mg cloprostenol)

Preservative:

Benzyl alcohol 20 mg

A list of inactive ingredients is detailed in section 13 – “Further information”.

3. What is the medicinal product intended for:

Estrumate Veterinary is a solution with potent luteolytic characteristics, causing morphological and functional regression of the corpus luteum in cattle and horses, followed by return to oestrus and normal ovulation.

Therapeutic group: Synthetic prostaglandin.

Estrumate Veterinary is a synthetic prostaglandin intended for use in cattle and horses. It is similar in structure to prostaglandin F2 alpha (PGF 2 alpha).

4. Contraindications:

Do not administer Estrumate Veterinary to pregnant animals unless the objective is to terminate pregnancy.

5. Side effects:

In very rare cases (less than one animal in 10,000 animals, including isolated reports), anaphylactic-type reactions can be observed which require immediate medical care.

On rare occasions (more than one animal but less than 10 in 10,000 animals), severe life-threatening local bacterial infections may occur associated with clostridial proliferation at the injection site. It is important to keep treated animals under observation and, if such infection occurs aggressive antibiotic therapy, particularly covering clostridial species, should be employed as a matter of urgency.

Careful aseptic techniques should be employed to decrease the possibility of these infections.

If you notice any serious side effects or other effects not mentioned in this consumer leaflet, please inform your veterinarian.

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects due to drug treatment" found on the Ministry of Health homepage (www.health.gov.il), that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il/>

6. Target species:

Cattle and horses

7. Method of administration and dosage:

Estrumate Veterinary must be administered intramuscularly.

Cattle: 2.0 ml

Ponies and donkeys: 0.5-1.0 ml

Heavy horses and thoroughbreds: 1.0-2.0 ml

8. How to use the medicinal product:

Due to the possibility of post-injection bacterial infections, careful aseptic techniques should be employed, while maintaining aseptic conditions. Do not inject into dirty or wet skin areas.

In cattle:

Treatment: A single intramuscular dose is very effective in the following situations:

Suboestrus: A condition observed in very high yielding cows, especially at peak lactation, and particularly in cows having good oestrous cyclicity but in which behavioral manifestations of oestrus are either very mild or absent. Such cows can be treated with Estrumate Veterinary following diagnosis of a corpus luteum by rectal examination. Cows showing indications of heat can be inseminated. Those cows which do not show heat should be examined after 11 days, and may be injected with a second dose and be bred at the time of oestrus.

Where re-examination is carried out 14 days later, animals should be inseminated on appearance of the second oestrus rather than at pre-fixed times.

Induction of parturition: Estrumate Veterinary will induce parturition on injection at the time around expected parturition. Parturition can be induced 10 days before the predicted calving date, or at about day 270 from the confirmed date of conception, except in urgent and pathological cases. All treated cows must receive close supervision.

Following induced early parturition, retention of the placenta is to be expected, as in other cases of induced early parturition.

Termination of normal pregnancy: Normal pregnancy can be terminated from one week after conception until the 150th day of pregnancy. Before 100 days of pregnancy, abortion can be induced rapidly and efficiently, while between 100 and 150 days of pregnancy results are less reliable, probably because of the fact that a certain percentage of the cows do not require the functioning of the corpus luteum for the maintenance of pregnancy. Do not attempt to induce abortion after 150 days of pregnancy.

Treated cows must be kept under observation until expulsion of the foetus and placenta is complete. Inducing abortion at a later stage is complicated and requires a different level of treatment.

Termination of abnormal pregnancy: Mummified foetus – Death of the foetus may be followed by its dehydration and disintegration.

Use of Estrumate Veterinary at any stage of pregnancy will result in the expulsion of the foetus from the uterus into the vagina from where it should be removed manually. Normal cyclical activity should then follow.

Hydrops of the foetal placenta – Hydramnios and hydrallantois can cause physiological complications and death of the foetus. Surgical intervention is not always effective. A single injection of Estrumate Veterinary can induce parturition in such cases, particularly in the first period (up to six months) of pregnancy.

Chronic endometritis (Pyometra) – This condition may be successfully treated with a single injection of Estrumate Veterinary. In particularly difficult cases, treatment may be repeated after 10-14 days.

Ovarian cysts – Estrumate Veterinary may be used where ovarian cysts are associated with the corpus luteum, and absence of heat is diagnosed. Estrumate Veterinary will bring about a return to regular cyclicity.

Synchronized oestrus: Estrumate Veterinary may be used to synchronize oestrus in cattle. A variety of treatment regimens exists for this purpose, and the most appropriate for each herd should be selected. Individuals or different groups of animals can be synchronized, as required. Estrumate can be used to complement oestrus detection, or insemination may be undertaken according to a breeding schedule without reference to the natural oestrus of the cows.

Programs for synchronized oestrus:

Examples of synchronized oestrus:

1. A single Estrumate Veterinary treatment of cows having undergone a rectal examination for evidence of a corpus luteum, followed by insemination on appearance of oestrus.
2. Detection of oestrus for 6 days and then insemination of those cows seen in heat. A single treatment is given to those cows not displaying signs of oestrus within 6 days, followed by insemination of the cows with appearance of oestrus.
3. Two injections of Estrumate Veterinary 11 days apart, then insemination at the next oestrus or at prescheduled times (see below).
4. As 3 above, but inseminating/breeding any cow showing oestrus before the second injection. The second injection is only given to those cows not seen in oestrus during that time. Breeding of the cows is then either on signs of the next oestrus or at prescheduled times.

Cows that respond well to a single prostaglandin injection will normally display oestrus within 6 days. The response to a double injection is generally much more rapid. Any cow may be inseminated following the first signs of oestrus in any of the Estrumate Veterinary treatment programs, with the exception of prescheduled insemination, when insemination can only be undertaken following the second injection. In other cases, insemination can be performed either once at 72-84 hours or twice at 72 and at 96 hours after the second injection of Estrumate Veterinary, as

preferred. For successful treatment, cows should be cycling well. Rectal examination before treatment will preclude the treatment of non-cycling or pregnant cows. Attention should be directed to the diet and other conditions during treatment. Avoid sudden changes in feeding levels or in feed constituents, in housing and other factors, in order not to stress the cows. In cases of insemination, make sure that the semen and insemination technique are of good quality.

Control of the oestrous cycle is of value in:

Dairy herds:

- a. To control oestrus in the individual cow in order to provide an individual calving index and to reduce the number of cows culled as barren.
- b. To control oestrus in groups of cows in order to facilitate management of the herd in groups of suitable size and to maintain seasonal calving.
- c. To permit the use of insemination in dairy heifers to speed up the breeding program.

Beef herds:

- a. To facilitate insemination programs.
- b. To enable the most effective use of bulls, where natural breeding is preferred.
- c. To permit better management of conception and calving.

In horses:

The property of shortening the life-span of the corpus luteum makes Estrumate Veterinary very effective in a number of conditions in horses:

Induction of luteolysis following foetal death and resorption: About 8-10% of all mares which conceive lose the conceptus during the first 100 days of pregnancy. Persistence of luteal function precludes an early return to oestrus.

Termination of persistent oestrus: Non-pregnant mares spontaneously enter periods of temporary absence of oestrus (dioestrus), particularly in the latter part of the breeding season (a condition different to anoestrus).

Termination of pseudopregnancy: There are cases in which covered mares display clinical signs of pregnancy but they are not actually pregnant.

Treatment of lactation anoestrus: Absence of oestrus for several months in mares after lactating or in pseudoestrus can be avoided.

Establishing oestrous cycles in barren mares: Some of the mares will be found on examination to have a functional corpus luteum and are suffering from abnormal persistence of a corpus luteum or are failing to exhibit normal oestrous behavior ("silent or hidden heat").

Facilitation of stud management: Mares may be brought into oestrus on a planned timing schedule either singly or in groups, to facilitate more efficient use of stallions.

9. Withdrawal periods:

Withdrawal period for meat: 24 hours.

Withdrawal period for milk: zero milkings.

Estrumate Veterinary is not to be used in horses intended for human consumption.

10. Warnings:

- Special warnings relating to the safety of use of the medicine in animals
Do not administer intravenously.
- Special warnings relating to the use of the medicine in treatment of the target animal
There is a gap of 4-5 days after ovulation when cattle and horses are insensitive to the luteolytic effect of prostaglandins.
- Special warnings relating to the safety of the person administering the medicinal product
Avoid direct contact with the skin or mucous membranes of the user.
Prostaglandins of the F2 α type may be absorbed through the skin and **may cause bronchospasm or a miscarriage.**
Care should be taken when handling the product to **avoid self-injection or skin contact.**
Pregnant women, women of childbearing age, asthmatics and persons with other respiratory tract diseases should exercise extra caution when handling cloprostenol. These persons should avoid contact or wear disposable gloves during administration of the product.
In case of skin contact, wash immediately with soap and water.
The possible incidence of bronchospasm with the product is unknown.
In cases of breathing difficulties resulting from inhalation or injection, immediately seek urgent medical attention and show the doctor this warning.
Wash hands after use.
- Pregnancy and lactation of the treated animal
Do not administer the preparation to pregnant animals unless the object of treatment to terminate pregnancy.
Estrumate Veterinary has a high margin of safety and does not impair fertility.
No unusual occurrences have been detected in offspring born following use of Estrumate Veterinary.
- Interactions with other medicinal products and other types of interaction
None described
- Overdose:
Cattle:
At 5 to 10 times the accepted dosage, the most frequent side effect is increased rectal temperature. This effect is usually transient and not detrimental to the animal. Limited salivation may also be observed in some animals.
Horses:
The most frequent side effects are sweating and decreased rectal temperatures. These effects are usually transient and not detrimental to the animal. Other possible effects may be increased heart rate, increased respiratory rate, abdominal discomfort, locomotor incoordination and lying

down. If these effects occur, they will be seen within 15 minutes of injection and disappear within an hour following injection. Mares usually continue to eat throughout.

- **Incompatibilities**
Strong acid/alkaline products.

11. Instructions for storage:

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 30°C.
Protect from light.
- After first opening, use within 28 days.

12. Instructions regarding disposal of the medicinal product/remnants of the medicinal product after use:

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of as toxic waste, do not throw to sewer.

13. Further information:

- In addition to the active ingredient, the medicine also contains:
Benzyl alcohol, Citric acid, Sodium citrate, Sodium chloride, Water for injection.
- What the medicine looks like: A clear, colourless, aqueous solution.
- Contents of the package: Multidose vials containing 10 or 20 ml.
- **Registration holder and its address:**
Intervet Israel Ltd., Industrial zone Neve Ne'eman, Hod Hasharon 45240.
- **Manufacturer name and its address:**
Vet-Pharma Friesoythe, Sedelsbergerstrasse 2, 26169 Friesoythe, Germany
- Revised in February 2021 according to MOHs guidelines.
- **Registration number of the medicinal product in the National Drug Registry of the Ministry of Health: 083-24-92156-00**