SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Lutalyse 12.5 mg/ml solution for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Dinoprost 12.5 mg (as Dinoprost tromethamine)

Excipient:
Benzyl alcohol 16.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear colourless to pale yellow solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle

4.2 Indications for use, specifying the target species

Lutalyse is indicated for its luteolytic and/or oxytocic effects in cattle. The indications for use are:

1. To more effectively control the time of oestrus in cycling cows.
2. To treat cows which have a functional corpus luteum, but do not express behavioural oestrus (sub-oestrus or silent heat).
3. To induce abortion.
4. To induce parturition.
5. For treatment of chronic metritis and pyometra.
6. For controlled breeding in normally cycling dairy cows:

- oestrus synchronisation
- ovulation synchronisation in combination with GnRH or GnRH analogues as part of fixed time artificial insemination protocols.

4.3 Contraindications

Do not use in animals suffering from either acute or sub-acute disorders of the vascular system, gastro-intestinal tract or respiratory system.

Do not use when abortion or parturition is not intended.
Do not administer by the intravenous route.

4.4 Special warnings for each target species

For intramuscular use in cattle only. Do not administer more than 2 ml per single injection
Lutalyse is ineffective when administered prior to day five after ovulation.
Administration of Lutalyse to cattle within four days after oestrus is unlikely to result in luteolysis of the corpus luteum.
Administration within 48 hours before onset of the next oestrus may not influence the timing of the oestrus after treatment.

4.5 Special precautions for use

Special precautions for use in animals

1. Animals should not be treated if they suffer from either acute or sub-acute disorders of the vascular system, gastro-intestinal tract or respiratory system.
2. Pregnancy status should be determined prior to injection since Lutalyse has been demonstrated to result in abortion or parturition induction when administered at sufficiently high doses to many animal species.
3. 4. If pregnant, the unlikely possibility of uterine rupture should be borne in mind, especially if cervical dilation does not occur.
5. Careful aseptic techniques should be employed to decrease the possibility of post injection bacterial infections.

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

1. Prostaglandins of the F2α type may cause bronchospasm or miscarriage.
2. These substances can be absorbed through the skin, so care should be taken when handling the product to AVOID SELF-INJECTION or SKIN CONTACT.
3. Pregnant women, women of child-bearing age, asthmatics and those with bronchial or other respiratory problems should avoid contact with the product.
4. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
5. Avoid contact with the eyes. In case of accidental contact with eyes, rinse immediately with plenty of water.
6. Accidental spillage on the skin should be washed off immediately with soap and water.
7. Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Small, firm swellings at the injection site (with no associated erythema, heat or sensitivity) have been reported very rarely in spontaneous reports after intramuscular administration of the product. These can take up to 9 days to resolve.

Localised post injection bacterial infections that may become generalised have been reported very rarely post-authorisation. Aggressive antibiotic therapy, particularly covering clostridial species, should be employed at the first sign of infection.

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

Termination of pregnancy is an indication for use.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

The dose for all indicated use in cattle is 2 ml (25 mg dinoprost).

A single injection of the recommended dose of dinoprost activity is luteolytic provided a functional corpus luteum is present.

Administer by intramuscular injection. Full aseptic precautions must be taken. Use a sterile syringe and needle and make the injection through an area of clean dry skin. Care should be taken to avoid injection through wet or dirty areas of skin.

The rubber stopper of the vial may be safely punctured up to 20 times. Otherwise, automatic syringe equipment, or a suitable draw-off needle, should be used for the 100 ml vials to avoid excessive puncturing of the closure.

NOTES

1. Oestrus control in cycling cattle.

Individual cows or heifers treated during dioestrus will normally return to oestrus and ovulate within two or four days after treatment. This may be employed to advantage as an effective aid towards managing oestrus and breeding in individual animals.

2. Treatment of sub-oestrus (no visible oestrus) in cattle.

Individual cattle may have normal cyclical ovarian activity, without detectable behavioural oestrus; this occurs most frequently in the winter months, at peak lactation in high producing dairy cows and in suckler beef cows. If a corpus luteum is present and ovulation has not occurred in the previous four days, administration of Lutalyse will result in corpus luteum regression followed by return to oestrus and ovulation.

Breeding of cattle treated with Lutalyse for the above indication may be by natural service, artificial insemination at the usual time in relation to observed oestrus, or by fixed time insemination (78 hours or 72 and 90 hours post-treatment).

3. Induction of abortion in cattle.

Lutalyse may be used to terminate pregnancy in cattle through its luteolytic effect during those stages of pregnancy in which the corpus luteum is sensitive to its action and in which maintenance of pregnancy is dependent upon the corpus luteum as the sole source of progesterone.

Stage of gestation in cattle is an important factor influencing response. The percentage of animals responding to a single intramuscular injection decreases as the gestation period increases. Approximate percentage responding are 90% within the first 100 days of gestation, 60% within 101-150 days of gestation and 40% in animals beyond 150 days of gestation. In the early stages of gestation, abortion will usually occur within one week, but as gestation length increases, the period to abortion following injection may also increase.

4. Induction of parturition in cattle.

Lutalyse has been used to induce parturition on or after day 270 of gestation. The interval from administration to parturition is one to eight days (average three days). Induction of parturition in cattle is indicated where there is a risk of oversize calves or where early parturition is desired. In addition, induction is indicated where pregnancies are complicated by miscellaneous conditions such as mummified or macerated foetuses, hydrops amnii, hydroallantois, etc. Lutalyse is indicated for expulsion of a dead foetus.

5. Treatment of metritis or pyometra in cattle.

In the cow chronic metritis frequently occurs as a sequel to an acute or sub-acute endometritis in the first two or three weeks post-partum; typically, there is an intermittent purulent or mucopurulent discharge. Pyometra is characterised by the retention of purulent fluid within the uterus.

Luteal regression through the administration of Lutalyse is followed by oestrus, during which the uterine environment is relatively unfavourable to the bacteria involved in the infection. Treatment may have to be repeated after 10-12 days where the condition is long standing.

6. Controlled breeding in cattle.

Lutalyse is indicated for its luteolytic effect in cattle. This luteolytic effect can be utilised to control the timing of oestrus in cycling cattle that have a corpus luteum. For normally-cycling cows, at least 35 days after calving, the identified activity of Lutalyse permits a wide range of oestrus control programmes.

Programme I

1. Inject 2 ml Lutalyse 12.5 mg/ml (25 mg dinoprost) intramuscularly;
2. Repeat the injection in 11 (10 to 12) days; then,
3. Inseminate 78 (75 to 80) hours after the second Lutalyse injection. No oestrus detection or observation is required if animals were cycling normally when injected.

This programme is recommended for most herds with successful A.I experience where females are known to be cycling.

Programme II

1. Inject 2 ml Lutalyse 12.5 mg/ml (25 mg dinoprost) intramuscularly;
2. Repeat the injection in 11 (10 to 12) days; then,
3. Inseminate 72 (70 to 74) hours and 90 (88 to 96) hours after the second Lutalyse injection. No oestrus detection or observation is required if animals were cycling normally when injected.

Double insemination has demonstrated increased pregnancy rates in some herds.

Programme III[a]

1. Inject 2 ml Lutalyse 12.5 mg/ml (25 mg dinoprost) intramuscularly;
2. Repeat the injection in 11 (10 to 12) days; then,
3. Inseminate upon detected oestrus.

Programme IV[a]

1. Inject 2 ml Lutalyse 12.5 mg/ml (25 mg dinoprost) intramuscularly;
2. Inseminate upon detected oestrus.

a If it is unknown whether most animals to be treated are cycling, Programmes III and IV calling for oestrus detection should be followed rather than Programmes I and II calling for timed insemination. A "clean-up bull" may be used following any Lutalyse programme, or the service may be repeated at the next oestrus, one cycle later, in animals that did not conceive at first service.

Practical application of these programmes will vary depending upon many factors, and in many cases these programmes may be altered to meet the requirements of the specific operation. For example, some veterinary surgeons may wish to design their own programmes for specific situations and schedules. The activity of Lutalyse may be easily adapted for such individualised approach. These changes should be carefully evaluated to ensure that they do not detrimentally affect the success of the breeding programme.

Programme V

Lutalyse may be used as part of a fixed time artificial insemination protocol to synchronise ovulation for normally-cycling dairy cows at any stage of lactation. The following protocols have been commonly reported in the literature:

- Day 0 – Inject GnRH or analogue
- Day 7 – Inject 2 ml Lutalyse 12.5 mg/ml (25 mg dinoprost) intramuscularly
- Day 9 – Inject GnRH or analogue
- Artificial insemination 16–20 hours later or at observed oestrus if sooner.

Alternatively:

- Day 0 – Inject GnRH or analogue
- Day 7 – Inject 2 ml Lutalyse 12.5 mg/ml (25 mg dinoprost) intramuscularly
- Artificial insemination and inject GnRH or analogue 60–72 hours later or at observed oestrus if sooner.

To maximise conception rates of cows to be treated, the ovarian status should be determined, and regular cyclic ovarian activity confirmed. Optimal results will be achieved in healthy normally-cycling cows.

GENERAL NOTES

Many factors contribute to the success and failure of reproduction management, and these are important when the time of breeding is to be regulated with Lutalyse. Some of these factors are:

1. Cattle must have a corpus luteum on the ovary of about five days or more of age in order for Lutalyse to be luteolytic, i.e. they are healthy and are undergoing normal oestrus cycles.
2. Semen of high fertility must be inseminated.
3. Semen must be inseminated properly.
4. Oestrus must be detected accurately if timed AI is not employed.
5. Physical facilities must be adequate to allow cattle handling without being detrimental to the animal.
6. Nutritional status must be adequate prior to and during the breeding season as this has a direct effect on conception and the initiation of oestrus in heifers or return of oestrus cycles in cows following calving.

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

The most frequently observed side-effect is increased rectal temperature at a 5x or 10x overdose. However, rectal temperature changes have been transient in all cases observed and have not been detrimental to the animal. Limited salivation has been seen in some instances.

4.11 Withdrawal period(s)

Cattle (meat & offal): 2 days
Cattle (milk): Zero hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Prostaglandins
ATCvet code: QG02AD01

5.1 Pharmacodynamic properties

The therapeutic use of dinoprost (natural prostaglandin F2a) in food producing animals is to induce regression of corpora lutea. This response is observed in many animals. The intracellular mechanism by which dinoprost induces luteolysis remains unknown. Various other physiological responses to dinoprost are known. These include stimulation of smooth muscle including vascular, bronchial, uterine and gastrointestinal muscle.

5.2 Pharmacokinetic particulars

Following administration, dinoprost tromethamine is rapidly dissociated to dinoprost (PGF2a). This compound has an extremely short blood half-life of only a few minutes. Near complete clearance occurs on one to two passages through the liver or lungs. No accumulation of dinoprost or residues have been observed in blood following repeated daily injections in cattle. Highest tissue concentrations of dinoprost are observed at the injection site which deplete to background concentrations by 24-48 hr post-injection. Residue concentrations in milk of cows peak at 2 hr post-injection and decrease rapidly thereafter.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
Sodium Hydroxide (for pH adjustment)
Hydrochloric Acid (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

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Type I glass vial with a chlorobutyl rubber stopper and an aluminium seal with flip-off disc.
Cardboard box containing one 10 ml, 20 ml or 100 ml vial.

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

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

8. MARKETING AUTHORISATION NUMBER

Vm 42058/4189

9. DATE OF FIRST AUTHORISATION

02 December 2015

10. DATE OF REVISION OF THE TEXT

April 2021

Approved: 07/04/21