Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

**DESCRIPTION**

LUTALYSE® Injection (5 mg dinoprost/mL) is a sterile solution containing the naturally occurring prostaglandin F2 alpha (dinoprost) as the tromethamine salt. Each mL contains dinoprost tromethamine equivalent to 5 mg dinoprost also, benzyl alcohol, 16.5 mg added as preservative. When necessary, pH was adjusted with sodium hydroxide and/or hydrochloric acid. Dinoprost tromethamine is a white or slightly off-white crystalline powder that is readily soluble in water at room temperature in concentrations to at least 200 mg/mL.

**INDICATIONS FOR USE**

Cattle: LUTALYSE Injection is indicated as a lutecytic agent. LUTALYSE Injection is effective only in those cattle having a corpus luteum, i.e., those which ovulated at least five days prior to treatment. Future reproductive performance of animals that are not cycling will be unaffected by injection of LUTALYSE Injection.

- For estrus synchronization in beef cattle and non-lactating dairy heifers
- For unobserved (silent) estrus in lactating dairy cows with a corpus luteum
- For treatment of pyometra (chronic endometritis) in cattle
- For abortion of foetid and other non-lactating cattle
- For use with FACTREL (gonadorelin injection) Injection to synchronize estrous cycles to allow fixed-time artificial insemination (FTAI) in lactating dairy cows
- For use with EA-ZI-BREED™ CIDR (progesterone intravaginal insert) Cattle Insert for synchronization of estrus in lactating dairy cows
- For use with EA-ZI-BREED™ CIDR (progesterone intravaginal insert) Cattle Insert for synchronization of estrus in suckled beef cows and replacement beef and dairy heifers, advancement of first postpartum estrus in suckled beef cows, and advancement of first postpartum estrus in beef heifers

**DOGS AND ADMINISTRATION**

As with any multi-dose, viable, aseptic techniques in withdrawing each dose to decrease the possibility of post-injection bacterial infections. Adequately clean and disinfect the vial stopper prior to entry with a sterile needle and syringe. Use only sterile needles, and use each needle only once. No vial stopper should be entered more than 20 times. For this reason, the 100 mL bottle should only be used for cattle. The 30 mL bottle may be used for cattle, swine, or mares.

**Cattle**

1. For Estrus Synchronization in Beef Cattle and Non-Lactating Dairy Heifers: LUTALYSE Injection is used to control the timing of estrus and ovulation in estrous cycling cattle that have a corpus luteum. Inject a dose of 5 mL LUTALYSE Injection (25 mg dinoprost) intramuscularly either once or twice at a 10 to 12 day interval. With the single injection, cattle should be bred at the usual time relative to estrus. With the two injections, cattle can be bred after the second injection either at the usual time relative to detected estrus or at about 80 hours after the second injection of LUTALYSE Injection. Estrus is expected to occur 1 to 5 days after injection if a corpus luteum was present. Cattle that do not become pregnant to breeding at estrus on days 1 to 5 after injection will be expected to return to estrus in about 18 to 24 days.

2. For Unobserved (silent) Estrus in Lactating Dairy Cows with a Corpus Luteum: Inject a dose of 5 mL LUTALYSE Injection (25 mg dinoprost) intramuscularly. Breed cows as they are detected in estrus. If estrus has not been observed by 80 hours after injection, breed at 80 hours. If the cow returns to estrus, breed at the usual time relative to estrus.

**Management Considerations:**

- Factors contribute to success and failure of reproduction management. Some of these factors are:
  - Cattle must be ready to breed—they must have a corpus luteum and be healthy;
  - Nutritional status must be adequate as this has a direct effect on conception and initiation of estrus in heifers or return of estrous cycles in cows following calving;
  - Physical facilities must be adequate to allow cattle handling without being detrimental to the animal;
  - Estrus must be detected accurately if timed AI is not employed;
  - Sire of high fertility must be used;
  - Females must be inseminated properly.

A successful breeding program can employ LUTALYSE Injection effectively, but a poorly managed breeding program will continue to be poor when LUTALYSE Injection is employed unless other management deficiencies are remedied first. Cattle expressing estrus following LUTALYSE Injection are receptive to breeding by a bull. Using bulls to breed large numbers of cattle in heat following LUTALYSE Injection will require proper management of the herd.

3. For Treatment of Pyometra (chronic endometritis) in Cattle: Inject a dose of 5 mL LUTALYSE Injection (25 mg dinoprost) intramuscularly.

4. For Abortion of Feedlot and Other Non-Lactating Cattle: LUTALYSE Injection is indicated for its abortifacient effect in feedlot and other non-lactating cattle during the first 100 days of late gestation. In late gestation.

5. For use with FACTREL® (gonadorelin injection) Injection to synchronize estrous cycles to allow fixed-time artificial insemination (FTAI) in lactating dairy cows: Administer 2 to 4 mL FACTREL Injection (100-200 mcg gonadorelin) per cow as an intramuscular injection in a treatment regimen with the following framework:

   - Administer the first dose of FACTREL Injection (2-4 mL) at Day 0
   - Administer LUTALYSE (25 mg dinoprost, as dinoprost tromethamine) Injection by intramuscular injection 6-8 days after the first dose of FACTREL Injection.
   - Administer a second dose of FACTREL Injection (2-4 mL) 30 to 72 hours after the first dose of LUTALYSE Injection.
   - Perform FTAI 0 to 24 hours after the second dose of FACTREL Injection, or inseminate cows on detected estrus using standard herd practices.

6. For use with EA-ZI-BREED™ CIDR (progesterone intravaginal insert) Cattle Insert for Synchronization of Estrus in Lactating Dairy Cows:

   - Administer one EA-ZI-BREED CIDR Cattle Insert per animal and remove 7 days later (for example, administered on a Monday remove the following Monday).
   - Administer 5 mL LUTALYSE Injection at the time of removal of the EA-ZI-BREED CIDR Cattle Insert.
   - Observe animals for signs of estrus on Days 2 to 5 after removal of the EA-ZI-BREED CIDR Cattle Insert and inseminate animals found in estrus following normal herd practices.

7. For use with EA-ZI-BREED™ CIDR (progesterone intravaginal insert) Cattle Insert for synchronization of estrus in suckled beef cows and replacement beef and dairy heifers, advancement of first postpartum estrus in suckled beef cows, and advancement of first postpartum estrus in beef heifers:

   - Administer one EA-ZI-BREED CIDR Cattle Insert per animal for 7 days (for example, if administered on a Monday remove the following Monday).
   - Inject 5 mL LUTALYSE Injection (equivalent to 5 mg/mL dinoprost) 1 day prior to EW-10 CIDR Cattle Insert removal on Day 6 of the 7 day administration period.
   - Observe animals for signs of estrus on Days 1 to 3 after removal of the EA-ZI-BREED CIDR Cattle Insert and inseminate animals about 12 hours after onset of estrus.

**Swine:**

For Intramuscular use for parturition induction in swine. LUTALYSE Injection is indicated for parturition induction in swine when injected within 3 days of normal predicted farrowing. The response to treatment varies by individual animals with a mean interval from administration of 2 mL LUTALYSE Injection (10 mg dinoprost) to parturition of approximately 30 hours. This can be employed to control the timing of farrowing in sows and gilts in late gestation.

**Management Considerations:** Several factors must be considered for the successful use of LUTALYSE Injection for parturition induction in swine. The product must be administered at a relatively specific time (treatment earlier than 3 days prior to normal predicted farrowing may result in increased piglet mortality). It is important that adequate records be maintained on (1) the average length of gestation period for the animals on a specific location, and (2) the breeding and projected farrowing dates for each animal. This information is essential to determine the appropriate time for administration of LUTALYSE Injection.

**Mares:**

LUTALYSE Injection is indicated for its luteocytic effect in mares. Administer a single intramuscular injection of 1 mg per 100 lbs (45.5 kg) body weight which is usually 1 mL to 2 mL LUTALYSE Injection. This luteocytic effect can be utilized to control the timing of estrus in the cycling and clinically anestrous mares that have a corpus luteum in the following circumstances:

1. **Controlling Time of Estrus of Estrous Cycling Mares:** Mares treated with LUTALYSE Injection during diestrus (4 or more days after ovulation) will return to estrus within 2 to 4 days in most cases and ovulate 8 to 12 days after treatment. This procedure may be utilized as an aid to scheduling the use of stallions.

2. **Difficult-to-Breed Mares:** In extended diestrus there is failure to exhibit regular estrous cycles which is different from true anestrus. Many mares described as anestrus during the breeding season have serum progesterone levels consistent with the presence of a functional corpus luteum. A proportion of “barren”, maiden, and lactating mares do not exhibit regular estrous cycles and may be in extended diestrus. Following abortion, early fetal death and resorption, or as a result of “pseudopregnancy”, there may be serum progesterone levels consistent with a functional corpus luteum. Treatment of such mares with LUTALYSE Injection usually results in regression of the corpus luteum followed by estrus and/or ovulation. Treatment of “anestrus” mares which abort subsequent to 36 days of pregnancy may not result in return to estrus due to presence of functional endometrial cups.

**WARNINGS AND PRECAUTIONS**

**User Safety:** Not for human use. Keep out of the reach of children. Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. In the early stages, women may be unaware of their pregnancies. Dinoprost tromethamine is readily absorbed through the skin and can cause abortion and/or bronchospasms. Accidental spillage on the skin should be washed off immediately with soap and water.

To report suspected adverse events, for technical assistance or to obtain a copy of the Material Safety Data Sheet (MSDS) contact Zoetis Inc. at 1-888-963-8471. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVets/SafetyHealth.

**Residue Warnings:** No milk discard or preslaughter drug withdrawal period is required for labeled uses in cattle. No preslaughter drug withdrawal period is required for labeled uses in swine. Use of this product in excess of the approved dose may result in drug residues. Do not use in horses intended for human consumption.

**Animal Safety Warnings:** Severe localized cleriodial infections associated with injection of LUTALYSE Injection have been reported. In rare instances, such infections have resulted in death. Aggressive antibiotic therapy should be employed in the first sign of infection on the injection site whether localized or diffuse. Do not administer intravenously (IV) as this route may potentiate adverse reactions. Non-steroidal anti-inflammatory drugs may inhibit prostaglandin synthesis; therefore this class of drugs should not be administered concurrently. Do not administer to pregnant cattle, unless abortion is desired. Cattle administered a progestin would be expected to have a reduced response to LUTALYSE Injection. Do not administer to sows and/or gilts prior to 3 days of normal parturition.
predicted farrowing as an increased number of stillbirths and postnatal mortality may result. In mares, LUTALYSE Injection is ineffective when administered prior to day-5 after ovulation. Mare pregnancy status should be determined prior to treatment since LUTALYSE Injection has been reported to induce abortion and parturition when sufficient doses were administered. Mares should not be treated if they show signs of parturition or other systems need be established by the body to metabolize injected dinoprost. To report adverse reactions call Zoetis Inc. at 1-888-963-8471.

ADVERSE REACTIONS

Cattle: Limited salivation has been reported in some instances. Swine: The most frequently observed side effects were erythema and pruritus, slight incoordination, nesting behavior, itching, urination, defecation, abdominal muscle spasms, tail movements, hyperpnea or dyspnea, increased vocalization, salivation, and at the 100 mg (10x) dose only, possible vomiting. These signs were incoordination, lasting from 10 minutes to 3 hours, and were not detrimental to the health of the animal. Mares: The most frequently observed side effects are sweating and decreased rectal temperature. However, these effects were transient in all cases observed and have not been detrimental to the animal. Other reactions seen have been increase in heart rate, increase in respiratory rate, some abdominal discomfort, locomotor incoordination, and lying down. These effects are usually seen within 15 minutes of injection and disappear within one hour. Mares usually continue to eat during the period of expression of side effects. One anaphylactic reaction of several hundred mares treated with LUTALYSE Injection was reported but was not confirmed.

Contact Information: To report adverse reactions call Zoetis Inc. at 1-888-963-8471.

CLINICAL PHARMACOLOGY

General Biologic Activity: Prostaglandins occur in nearly all mammalian tissues. Prostaglandins, especially PGE2 and PGF2α, have been shown, in certain species, to 1) increase at time of parturition in amniotic fluid, maternal placenta, myometrium, and blood; 2) stimulate myometrial activity, and 3) to induce either abortion or parturition. Prostaglandins, especially PGF2α, have been shown to 1) increase in the uterus and blood to levels similar to levels achieved by exogenous administration with the use of a prostaglandin analog, luteolytic effect of crossing from the uterine vein to the ovarian artery (sheep); 3) be related to IUD induced luteal regression (sheep); and 4) be capable of regressing the corpus luteum of most mammalian species studied to date. Prostaglandins have been reported to result in release of pituitary tropic hormones. Data suggest prostaglandins, especially PGE2 and PGF2α, may be involved in the process of ovulation and gamete transport. Also PGF2α has been reported to cause increase in blood pressure, bronchoconstriction, and smooth muscle stimulation in certain species.

Metabolism: A number of metabolism studies have been done in laboratory animals. The metabolism of tritium labeled dinoprost (‘H PGF2α) in the rat and in the monkey was similar. Although quantitative differences were observed, qualitatively similar metabolites were produced. A study demonstrated that equimolar doses of ‘H PGF2α Tham and ‘H PGF2α free acid administered intravenously to rats demonstrated no significant differences in blood concentration of dinoprost. An interesting observation in the above study was that the radioactive dose of ‘H PGF2α alpha rapidly distributed in tissues and dissipated in tissues with almost the same curve as it did in the serum. The half-life of dinoprost in bovine blood has been reported to be on the order of minutes. A complete study on the distribution of decline of ‘H PGF2α alpha Tham in the tissue of rats was well correlated with the work done in the cow. Cattle serum collected during 24 hours after doses of 0 to 250 mg dinoprost have been assayed by RIA for dinoprost and the 15-keto metabolites. These data support previous reports that dinoprost has a half-life of minutes. Dinoprost is a natural prostaglandin. All systems associated with dinoprost metabolism exist in the body; therefore, no new metabolic, transport, excretion, binding or other systems need be established by the body to metabolize injected dinoprost.