FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

ANADA 200-253

ProstaMate™ (dinoprost tromethamine injection) Sterile Solution

For intramuscular use for estrus synchronization, treatment of unobserved (silent) estrus and pyometra (chronic endometritis) in cattle: for abortion of feedlot and other non-lactating cattle; for parturition induction in swine; and for controlling the timing of estrus in estrous cycling mares and clinically anestrous mares that have a corpus luteum.

Sponsored by:

Phoenix Scientific, Inc.
3915 South 48th Street Terrace
P.O. Box 6457
St. Joseph, MO 64506-0457
FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

ANADA Number: 200-253

Sponsor: Phoenix Scientific, Inc.
3915 South 48th Street Terrace
P.O. Box 6457
St. Joseph, MO 64506-0457

Generic Name: dinoprost tromethamine, USP

Trade Name: ProstaMate™ (dinoprost tromethamine injection) Sterile Solution

Dosage Form: injectable solution

How Supplied: 10 mL and 30 mL multiple dose vials

How Dispensed: Rx

Amount of Active Ingredients: Each mL contains 5 mg of dinoprost from dinoprost tromethamine

Route of Administration: IM Injection

Species: Cattle, swine, horses

Labeled Dosage: Cattle -5 mL IM
Swine -2 mL IM
Mares -1 mL IM

Indications for Use: For intramuscular use for estrus synchronization, treatment of unobserved (silent) estrus and pyometra (chronic endometritis) in cattle: for abortion of feedlot and other non-lactating cattle; for parturition induction in swine; and for controlling the timing of estrus in estrous cycling mares and clinically anestrous mares that have a corpus luteum.
2. **TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS**


For certain dosage forms, the agency grants a waiver from conducting an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990: *fifth GADPTRA Policy* Letter). In lieu of bioequivalence testing, the safety and efficacy of the generic product are based on the demonstrated chemical equivalence to the pioneer product.

Based upon the formulation characteristics of the generic product, Phoenix Scientific, Inc. was granted a waiver from conducting an *in vivo* bioequivalence study with ProstaMate™ (dinoprost tromethamine injection). The generic and pioneer products are solutions with the same active and inactive ingredients.

3. **HUMAN SAFETY**

**Human Food Safety**

Cattle: No Milk discard or preslaughter drug withdrawal period is required for labeled uses.

Swine: No preslaughter drug withdrawal period is required for labeled uses.

Mares: Not for use in horses intended for food.

**Human Safety Relative to Possession, Handling and Administration:**

The labeling contains adequate Warning statements, as described below.

Not for human use.

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 maybe unaware of their pregnancies. Dinoprost tromethamine is readily absorbed through the skin and can cause abortion and/or bronchospasms. Direct contact with the skin should, therefore, be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

4. **AGENCY CONCLUSION:**

This ANADA submitted under section 5 12(b) of the Federal Food, Drug and Cosmetic Act satisfies the requirements of section 512(n) of the Act and demonstrates that ProstaMate™ (dinoprost tromethamine injection) Sterile Solution, when used under the proposed conditions of use, is safe and effective for the labeled indications.
Attachments:

1. Generic Labeling:
   - Vial Label
   - Package Insert
   - Carton Label

2. Pioneer Labeling
   - Vial Label
   - Package Insert
   - Carton Label
See package insert for complete product information.
Each mL contains: dinoprost tromethamine equivalent to 5 mg dinoprost.
Warnings: Not for human use. Pregnant women, asthmatics, or persons with bronchial and other respiratory problems should avoid contact with dinoprost tromethamine. See package insert for additional information.
Note: Spills of ProstaMate™ on the skin should immediately be washed off with soap and water.
Restricted Drug-Use Only As Directed (California)
KEEP OUT OF REACH OF CHILDREN
Store at controlled room temperature 20°-25° C (68°-77° F).
Manufactured by
Phoenix Scientific, Inc.
St. Joseph, MO 64506
600092 Iss. 6-98
Lot No.
Exp. Date
Warnings: Not for human use. Pregnant women, asthmatics, or persons with bronchial and other respiratory problems should avoid contact with dinoprost tromethamine.

See package insert for additional information.

Note: Spills of ProstaMate on the skin should immediately be washed off with soap and water.

Restricted DrugUse Only AsDirected California

KEEP OUR OF REACH OF CHILDREN

Lot No.
Exp. Date

For intramuscular use for estrus synchronization, treatment of unobserved (silent) estrus and pyometra (chronic endometritis) in cattle; for abortion of foals and other non-breeding cattle; for pertussion induction in swine; and for controlling the timing of estrus in estrous cycling mares and clinically anestrous mares that have a corpus luteum.

See package insert for complete product information.

Store at controlled room temperature 20° to 25°C (68° to 77°F).

Manufactured by
Phoenix Biotechnology, Inc.
St. Joseph, MO 64507

Lot No.
Exp. Date

Net Contents: 30 mL
ProstaMate (dinoprost tromethamine injection)
Sterile Solution

Each mL contains: dinoprost tromethamine equivalent to 5 mg dinoprost, benzyl alcohol, 9.45 mg (as preservative), water for injection. The pH may be adjusted with sodium hydroxide and/or hydrochloric acid.

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See package insert for complete product information.

Store at controlled room temperature 20° to 25°C (68° to 77°F).

Manufactured by
Phoenix Biotechnology, Inc.
St. Joseph, MO 64507

Lot No.
Exp. Date
**Prosta* Mate**
(diospropantoic acid)

**Prostate health in a bottle**

**Description**

Prosta* Mate is a dietary supplement that contains specific nutrients designed to support prostate health and normal urinary function. It is formulated with a blend of ingredients that work synergistically to address common concerns related to prostate health, such as the need for increased urination, frequent nighttime trips to the bathroom, and a feeling of incomplete emptying.

**Ingredients**

Prosta* Mate contains the following key ingredients:

- **Diospropantoic Acid (DPA)**: A natural compound derived from palm fruit, which has been studied for its potential benefits in prostate health.
- **Zinc**:
- **Boron**:
- **Selenium**:
- **Vitamin D3**:

**Recommended Usage**

It is recommended to take 2 capsules daily, preferably with meals, to support healthy prostate function. However, it is always advisable to consult a healthcare professional before starting any new supplement regimen, especially if you have a pre-existing condition or are taking other medications.

**Side Effects**

Some common side effects associated with Prosta* Mate include:

- **Upset Stomach**
- **Nausea**

**Precautions**

If you are pregnant or breastfeeding, or have any medical condition, please consult your healthcare provider before using Prosta* Mate. It is also important to note that the product should not be used by children under the age of 18.

**Warnings**

- **Do not exceed the recommended dosage.**
- **Store in a cool, dry place.**
- **Keep out of reach of children.**

**DOSAGE AND ADMINISTRATION**

- Adults: 2 capsules daily, preferably with meals.
- Children: Use only under the supervision of a healthcare professional.

**Supplementary Information**

Prosta* Mate is not a substitute for professional medical advice. It is important to consult with a healthcare provider before starting any new supplement or making changes to your current medication regimen.

**Manufactured by**

Victor Healthcare, Inc.

**Supplied in**

- 30 Vegetable Capsules

**References**

1. The nutritional benefits of a healthy diet are well-documented and widely recognized.
2. Studies have shown that the intake of specific nutrients, like zinc, can support prostate health.
3. The role of antioxidants, such as vitamin D3, in maintaining overall health is also emphasized.

**Additional Resources**

For more detailed information about Prosta* Mate and its ingredients, please visit the manufacturer’s website or contact their customer support for further assistance.
For intramuscular use for estrus synchronization, treatment of undiagnosed (silent) estrus, pyometra (chronic endometritis) in cattle for abortion of feedlot and other non-lactating cattle, for parturition induction in swine, and for controlling the timing of estrus in estrous cycling mares and clinically anestrous mares that have a corpus luteum.

See package insert for complete product information.

Store at controlled room temperature 20° to 25°C (68° to 77°F) [see USP].

Warning: Not for human use. Pregnant women, asthmatics, or persons with bronchial and other respiratory problems should avoid contact with dinoprost tromethamine.

See package insert for additional information.

Note: Spills of LUTALYSE on the skin should immediately be washed off with soap and water.

Each mL contains: dinoprost tromethamine equivalent to 5 mg dinoprost; benzyl alcohol, 0.45 mg added as preservative.

When necessary, pH was adjusted with sodium hydroxide and/or hydrochloric acid.

For intramuscular use in cattle, swine, and mares.

Prostaglandin F2alpha for intramuscular use in cattle, swine, and mares.

Restricted Drug-use Only As Directed (California) For Use in Animals Only Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.
For intramuscular use for estrus synchronization, treatment of unobserved (silent) estrus and pyometra (chronic endometritis) in cattle; for abortion of feedlot gestations in non-lactating cattle; for parturition induction in swine; and for the control of the timing of estrus in estrous cycling mares and clinically anestrus mares that have a corpus luteum.

DESCRIPTION

This product contains the naturally occurring prostaglandin F2 alpha (dinoprost) as the tromethamine salt. Each mL contains dinoprost/tromethamine equivalent to 5 mg dinoprost also, benzyl alcohol, 9.45 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.

General Biologic Activity: Prostaglandins occur in nearly all mammalian tissues.

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Prostaglandins, especially PGE"s and PGF"s, have been shown, in certain species, to 1) increase at time of parturition, in amniotic fluid, maternal plasma, and/or blood, 2) stimulate myometrial activity, and 3) to induce either abortion or parturition. Prostaglandins, especially PGF2 alpha, have been shown to 1) increase uterine blood flow levels similar to levels achieved by exogenous administration which elicited luteolysis, 2) be capable of crossing the uterine vein to the ovarian artery (sheep), 3) be related to increased uterine velocity (sheep), and 4) be capable of eliciting a 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 PGE"s and PGF"s, may be involved in the process of ovulation and gamete transport. Also PGF2 alpha has been reported to cause increase in blood pressure, bronchoconstriction, and smooth muscle stimulation in certain species.

SAFETY AND TOXICITY

Laboratory Animals: Dinoprost was non-toxic in the rat when administered orally at 1, 25, 250, and 20,000 mg/kg/day for 1 day. It was orally and subcutaneously at 0.5 and 1.0 mg/kg/day for gestation days 6.7 and 8 or 9, 10 and 11, 12 and 13, and 14. Dinoprost was non-toxic in the rabbit when administered subcutaneously at doses of 0.3 and 1.0 mg/kg/day for gestation days 5.7 and 9 or 8, 10, and 11 or 12, 13, and 14. In rats, orally at doses of 0.01, 0.1, and 1.0 mg/kg/day on days 8-18 or 5.0 mg/kg/day on days 8-18 of gestation. A slight and marked embryo lethal effect was observed in dams given 1.0 and 5.0 mg/kg/day, respectively. This was due to the expected luteolytic properties of the drug.

A 14-day continuous intravenous infusion study in rats at 20 mg PGF2 alpha/kg body weight indicated prostaglandins of the F series could induce bone deposition. However, such bone changes were not observed in monkeys similarly administered LUTALYSE.

Sterile Solution at 15 mg Lutalyse® per kg body weight for 14 days.

Cattle: In cattle, evaluation was made of clinical observations, clinical chemistry, hematology, urinalysis, organ weights, and gross Plus microscopic measurements following treatment with various doses up to 2000 mg dinoprost administered twice intramuscularly at a 10 day interval or doses of 25 mg administered daily for 10 days. There was no unequivocal effect of dinoprost on the hematology or clinical chemistry parameters measured. Clinically, a slight transitory increase in heart rate was observed. Rectal temperature was elevated about 1.5° F through the 6th hour after injection with 250 mg dinoprost, but had returned to baseline at 24 hours after injection. An increase in eosinophils was detected. There was no evidence of toxicological effects. Thus, dinoprost was a safety factor of at least 100x on injection (25 mg luteolytic dose vs 250 mg luteolytic dose), based on studies conducted with cattle. At luteolytic dose, prostaglandin had no effect on pregnancy. In some cases, cows did not abort, the dose required for abortion varies considerably with the stage of gestation.

Induction of abortion in feedlot cattle at stages of gestation up to 100 days of gestation did not result in dystocia, retained placenta or death of the mother. In feedlot cattle, evaluation was made of clinical observations, clinical chemistry, hematology, urinalysis, organ weights, and gross microscopic observations following treatment with single doses of 10, 30, 50, and 100 mg dinoprost administered intramuscularly. The results indicated no treatment related effects from dinoprost treatment that were deleterious to the health of the animals or to their offspring.

Mares: Dinoprost/tromethamine was administered to adult mares (weighing 320 to 485 kg, 2 to 20 years of age) at the rates of 0, 100, 200, 400, and 800 mg per day for 6 days. Route of administration for each dose group was both intravenous (2 mares) and intramuscularly (2 mares). Changes were detected in all treated groups for clinical (reduced sensitivity to pain; locomotor incoordination; hyperemia; shivering; hyperthermia; labored respiration), blood chemistry (elevated cholesterol, total bilirubin, LDT, and glucose), and hematologic (decreased eosinophils, increased hemoglobin, hematocrit, and erythrocytes) measurements. The effects in the 100 mg dose, and to a lesser extent, the 200 mg dose groups were transient in nature, lasting for a few minutes to several hours. Mares did not appear to sustain adverse effects following termination of the study. No mortality occurred in any of the groups. No apparent differences were observed between the intramuscular and subcutaneous routes of administration. Luteolytic doses of dinoprost/tromethamine are in the order of 5 to 10 mg administered on one day, therefore, LUTALYSE was demonstrated to have a wide margin of safety. Thus, the 100 mg dose gave a safety margin of 10 to 20x for a single injection of 0.5 to 1.0 mg/day for daily administrations.

Additional studies investigated the effects in the mare of single intramuscular doses of 0, 0.25, 0.5, 1.0, 2.5, 3.0, 5.0, and 10.0 mg dinoprost/tromethamine. Heart rate, respiration...
for doses of 2.5, 3.0, 5.0, and 10.0 mg dinoprost tromethamine (TPF 2-alpha, or TPF 2, respectively) within 3 days of normal pregnancy

Additional studies investigated the effects in the mare of single intramuscular doses of 0.25, 1.0, 2.5, 3.0, 5.0, and 10.0 mg dinoprost tromethamine on uterine tone, rectal temperature, and sweating were measured at 0, 0.25, 0.50, 0.75, 1.0, 1.5, 2.0, 3.0, 4.0, 5.0, and 6.0 hr after injection. Neither heart rate nor respiration rates were significantly altered (P > 0.05) when compared to controls. High rectal temperatures were observed for 0, 0.75, 1.0, 1.5, 2.0, 3.0, 4.0, and 5.0 hr after injection. Mares treated with 2.5, 3.0, 5.0, and 10.0 mg dinoprost tromethamine (TPF 2) were markedly symptomatic. In all cases and was used for doses of 3.0 mg or less (usually 1 mg) for 5 minutes after the injection. The 10 mg dose was intermediate between that seen for mares treated with 3.0 and 10.0 mg. Sweating began within 15 minutes after injection and ceased by 45 to 60 minutes after injection. Rectal temperature was decreased during the first 10 hr and was lower than the control level at 15 to 20 hr after injection for 0.25 and 1.0 mg, 2.5, 3.0, or 5.0 mg and 10.0 mg dose groups, respectively. Average rectal temperature during the periods of decreased temperature was of the order of 97.5 ± 0.6 with the greatest decreased observed in the 10 mg dose group.

METABOLISM

A number of metabolism studies have been done in laboratory animals. The metabolism of trilium labeled dinoprost (TPF 2-alpha) in the rat and in the monkey was similar. Although quantitative differences were observed, qualitatively similar metabolites were identified. A study demonstrated that equine doses of TPF 2-alpha, TPF 2-alpha free acid administered intravenously to rats demonstrated no significant differences in blood concentration of TPF 2-alpha. An interesting finding in this study was that the radioactive dose of TPF 2-alpha rapidly distributed in tissues and dissipated in tissues with almost the same curve as did in the serum. The half-life of dinoprost in bones has been reported as about 20 minutes. A comparative study on the distribution of decline of TPF 2-alpha, in tissues 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 elements need to be established by the body to metabolize injected dinoprost.

INDICATIONS AND INSTRUCTIONS FOR USE

Cattle: LUTALYSE Sterile Solution is indicated as a luteolytic agent.

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

1. For Intramuscular Use for Estrus Synchronization in Beef Cattle and Non-Lactating Dairy Heifers. LUTALYSE 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 (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.

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 Intramuscular Use for Unobserved (Silent) Estrus in Lactating Dairy Cows with a Corpus Luteum. Inject a dose of 0.5 mL LUTALYSE (25 mg dinoprost) intramuscularly as estrus is detected in estrus. If estrus has not been observed by 80 hours after injection, breed at 80 hours. If the cow returns to estrus at the usual time relative to estrus.

Management Considerations: Many factors contribute to success and failure of reproduction management, and these factors are important also when time of breeding is to be regulated with LUTALYSE Sterile Solution. Some of these factors are:

a. Cattle must be ready to breed; they must have a corpus luteum and be healthy.

b. Nutritional status must be adequate; this has a direct effect on conception and the initiation of estrus in heifers or return of estrous cycles in cows following calving.

c. Physical facilities must be adequate to allow cattle handling without being detrimental to the animal.

d. Estrus must be detected accurately if timed AI is not employed.

e. Semen of high fertility must be used;

e. Semen must be inseminated properly.

A successful breeding program can employ LUTALYSE effectively, but a poorly managed breeding program will continue to be poor when LUTALYSE is employed. Several other management de facto are remedied first.

Cattle expressing estrus following LUTALYSE are receptive 10 breeding by a bull. Using bulls to breed large numbers of cattle in heat following LUTALYSE will require proper management of bulls and cattle.

3. For Intramuscular Use for Treatment of Pyometra (chronic endometritis) in Cattle. Inject a dose of 5 mL LUTALYSE (25 mg dinoprost) intramuscularly. In studies conducted with LUTALYSE, pyometra was defined as presence of a cervical or uterine mass in the ovary and uterine horns containing fluid but not a conceptus based on palpation per rectum. Return to normal was defined as evacuation of fluid and return of the uterine horns to normal or less than 40 mm in diameter or 40 mm or less when palpated per rectum at 14 and 28 days. Most cattle that recovered in response to LUTALYSE recovered within 14 days after injection. After 14 days, recovery rate of treated cattle was no different than that of control non-treated cattle.

4. For Intramuscular Use for Abortion of Feedlot and Other Non-Lactating Cattle. LUTALYSE is indicated for abortifacient effect in feedlot and other non-lactating cattle during the first 100 days of gestation. Inject a dose of 25 mg intramuscularly. Cattle that abort will abort within 35 days of injection.

Commercial cattle were palpated per rectum for pregnancy in sow feedlots. The percent of pregnant cattle in each feedlotless than 150 days of gestation was intermediate between 25 and 64; 50% or more of the pregnant cattle were less than 150 days of gestation. The abortion rate following injection of LUTALYSE increased with increasing doses up to about 25 mg. As examples, the abortion rates, over the dose titration study, were 22%, 50%, 71%, 93% and 78% for cattle treated up to 100 days of gestation when injected with LUTALYSE doses 3.0 (15 mg), 2.5 (10 mg), 2.0 (5 mg), 1.5 (4 mg) and 1.0 (2 mg) mL, respectively. The statistical predicted relative abortion rate based on the dose titration data, was about 93% for the 5 mL (25 mg) LUTALYSE dose for cattle injected up to 100 days of gestation.

SWINE: For intramuscular use for parturition induction in swine. LUTALYSE Sterile Solution is indicated for parturition induction in swine when injection is not normal predicted farrowing.

The response to treatment varies by individual animals with a mean interval from administration of 2 mL LUTALYSE (10 mg dinoprost) to parturition of approximately 30 hours. This can be employed to control the time of farrowing in sows and gilts in late gestation. Management Considerations: Several factors for successful use of LUTALYSE Sterile Solution for parturition induction in swine. The product must be administered at a relatively specific time (treatment earlier than normal predicted farrowing may result in increased piglet mortality). It is important that accurate records be maintained on the average length of gestation, the usual date of parturition and the location of the specific location, and the breeding and predicted farrowing dates for each animal.

This information is essential to determine the appropriate time for administration of LUTALYSE.

Mares: LUTALYSE Sterile Solution is indicated for luteolytic effect in mares. This LUTALYSE effect can be utilized to control the timing of estrus in estrus 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 during estrus (4 or more days after ovulation) will return to estrus within 2 to 4 days in most cases and ovulate 6 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 estrus 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 estrus. Following abortion, early fetal death syndrome

(continued from above)

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 usually results in regression of the corpus luteum followed by estrus and/or ovulation. In one study with 122 Standardbred and Thoroughbred mares in clinical anestrus for an average of 58 days, treatment during the breeding season, behavioral estrus was detected in 81 percent at an average time of 3.7 days after injection with 5 mg LUTALYSE; ovulation occurred an average of 7.0 days after treatment. Of those mares bred, 99% were pregnant following an average of 1.4 services during that estrus.

Treatment of "anestrus" mares which abort subsequent to 38 days of pregnancy may not result in return to estrus due to presence of functional endometrial cups.

WARNINGS

Not for human use.

Women of child-bearing 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. Dinoprostone may be readily absorbed through the skin and can cause abortion and/or bronchospasms. Direct contact with the skin should, therefore, be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

Use of this product in excess of the approved dose may result in drug residues.

PRECAUTIONS

Cattle: Do not administer to pregnant cattle unless abortion is desired.

Do not administer Intravenously (I.V.), as this route might potentiate adverse reactions.

Cattle administered a progestogen would be expected to have a reduced response to LUTALYSE Sterile Solution.

Aggressive antibiotic therapy should be employed at the first sign of infection at the injection site whether localized or diffuse. As with all parenteral products careful aseptic technique should be employed to decrease the possibility of post injection bacterial infections.

Swine: Do not administer to Sows and for gilts prior to 3 days of normal predicted farrowing, as increased number of stillborn and postnatal mortality may result.

Mares: LUTALYSE Sterile Solution is ineffective when administered prior to day-5 after ovulation.

Pregnancy status should be determined prior to treatment, since LUTALYSE has been reported to induce abortion and parturition when sufficient doses were administered. Mares should not be treated if they suffer from either acute or subacute disorders of the vascular system, gastrointestinal tract, respiratory system, or reproductive tract.

Do not administer by Intravenous route.

Nonsteroidal anti-Inflammatory drugs (i.e., indomethacin) may inhibit prostaglandin synthesis, therefore these drugs should not be administered concurrently.

ADVERSE REACTIONS

Cattle:

1. The most frequently observed side effect is increased rectal temperature at a 5X or 10X overdose. However, rectal temperature change has been transient in all cases observed and has not been detrimental to the animal.

2. Limited salivation has been reported in some instances.

3. Intravenous administration might increase heart rate.

4. Localized post injection bacterial infections that may become generalized have been reported. In rare instances such infections have terminated fatally. See PRECAUTIONS.

Swine: The most frequently observed side effects were anorexia, oliguria, 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 side effects are transitory, 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 have been 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, 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 exhibit period of expression of estrus effects. One anaphylactic reaction of several hundred mares treated with LUTALYSE Sterile Solution was reported but was not confirmed.

IMPORTANT

Cattle: No milk discard or preslaughter drug withdrawal period is required for labeled uses.

Swine: No preslaughter drug withdrawal period is required for labeled uses.

Mares: Not for use in horses intended for food.

DOSEAGE AND ADMINISTRATION

Cattle: LUTALYSE Sterile Solution is supplied at a concentration of 5 mg dinoprostone per mL. LUTALYSE Sterile Solution (125 mg/5 mL) administered intramuscularly. As with any multidose vial, practice aseptic techniques in withdrawing each dose. Adequately clean and disinfect the vial closure prior to entry with a sterile needle.

Swine: LUTALYSE Sterile Solution will induce parturition in swine at 10 mg/mL.
DOSAGE AND ADMINISTRATION

Cattle: LUTALYSE Sterile Solution is supplied at a concentration of 5 mg dinoprost per mL administered intramuscularly. As with any multidose vial, practice aseptic techniques in withdrawing each dose. Adequately clean and disinfect the vial closure prior to entry with a sterile needle.

Swine: LUTALYSE Sterile Solution will induce parturition in swine at 10 mg (2 mL) when injected intramuscularly.

with any multidose vial, practice aseptic techniques in withdrawing each dose. Adequately clean and disinfect the vial closure prior to entry with a sterile needle.

Mares: 1. Evaluate the reproductive status of the mare.
2. 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 Sterile Solution.
3. Observe for signs of estrus by means of daily teasing with a stallion, and evaluate follicular changes on the ovary by palpation of the ovary per rectum.
4. Some clinically anestrus mares will not express estrus but will develop a follicle which will ovulate. If inseminated at the appropriate time relative to rupture of the follicle, some clinically anestrus mares may become pregnant.
5. Breed mares in estrus in a manner consistent with normal management. Dinoprost tromethamine is administered once as a single intramuscular injection of 1 mg per 100 lbs (45.5 kg) body weight which is usually 1 mL to 2 mL of LUTALYSE containing 5 mg dinoprost as the tromethamine salt per milliliter.

HOW SUPPLIED

LUTALYSE Sterile Solution is available in 10 and 30 mL vials.

STORAGE CONDITIONS

Store at controlled room temperature 20° to 25°C (68° to 77°F) (see USP).

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

For further information, contact Upjohn Company, Kalamazoo, Michigan 49001, USA.

Revised August 1996

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