## **HEIFER BREEDING**

Simple steps to accelerate performance.

Lutalyse (dinoprost tromethan Sterile Solution



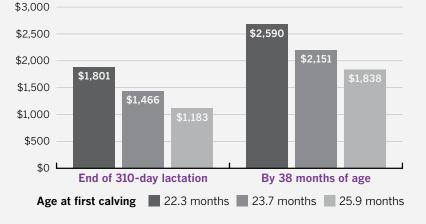


## Get heifers ready for work.

Heifers represent the best genetics within the herd, and ensuring they are bred and calve in a timely manner is crucial to future production. Research has shown long-term financial benefits to calving heifers for the first time at younger than 24 months of age.<sup>4</sup>

The decision to breed heifers to calve between 22 and 23 months of age needs to begin before they are ready for first insemination. Set goals and monitor growth to ensure replacement heifers are reaching breeding size targets by 12 to 13 months of age. Heifers must reach height and weight benchmarks to ensure a healthy calving and a smooth transition into higher production.

#### DISCOUNTED INCOME OVER FEED COSTS IS HIGHER FOR EARLIER AGE AT FIRST CALVING<sup>7</sup>



### Monitor performance.

Performance should be monitored on an ongoing basis. An important measure to track is age at first breeding. Set a goal for age at first insemination and see how many heifers are meeting it. Measurement of progress should be evaluated after each pregnancy check.

#### Building a better heifer.

Important steps must be taken early in a heifer's life to make sure she grows to her full potential.

**Timely feeding of colostrum** – Deliver 3 to 4 quarts of colostrum within six hours of birth

**High plane of nutrition** – Double a calf's birth weight and ensure appropriate structural growth by 60 days of age through a higher plane of nutrition pre-weaning

**Adequate housing** – Provide a clean, dry, well-ventilated place for calves to lie down

Monitor growth – Ensure calves are growing with routine measurement

# Calving heifers earlier reduces raising investments.

Heifers are an overlooked profit opportunity. According to industry estimates, it costs between \$1,595 and \$2,935 to raise a heifer from birth until freshening, one of the largest expenses on a dairy.<sup>1</sup>

Every month first calving is delayed beyond 22 months costs producers \$100 per heifer in lost milk production opportunity and additional raising costs.<sup>2</sup>

One way to reduce the investment in raising heifers is to calve heifers earlier. Age at first calving can be improved on most dairies. According to U.S. Department of Agriculture (USDA) research, age at first calving has averaged older than 25 months for the past 10 years despite industry recommendations and financial reasons to improve.<sup>3</sup>

Producers who routinely achieve an age at first calving between 22 and 24 months capture increased return on their heifer-raising investment in many different ways.

## Reduced raising costs

Earlier investment returns

Increased herd management flexibility

Fewer replacements on the dairy

Improving age at first calving reduces raising costs from birth to freshening  $^{\rm 1}$ 

Heifers that join the milking herd begin to return on raising investment earlier in life

Heifers entering the herd earlier can provide opportunities for expansion or voluntary culling

Heifers calving sooner reduce the total number of replacement heifers needed to meet herd size goals



# Improving heifer reproduction is simple.

Setting a goal for age at first calving won't ensure heifers are bred in time to reach it. Improving age at first calving takes a commitment to more aggressive management of heifer reproduction. Since gestation is a fixed length, first service conception risk and age at first breeding will be the biggest drivers of reproductive efficiency.

### Five easy steps.

There are real opportunities to move replacements into the milking herd sooner by taking simple steps to more aggressively manage heifer reproduction.

| 1. | Move heifers to the breeding pen.      | Heifers should be moved into the artificial insemination (AI) breeding pen as they reach height and weight targets and are ready for breeding. Don't delay based on age. If heifers are big enough, move them into the breeding pen.           |
|----|--|--|
| 2. | Use prostaglandin on date of move.     | Administer LUTALYSE <sup>®</sup> ( <i>dinoprost tromethamine</i> ) Sterile Solution on the day of movement and again 10 to 12 days later for heifers not yet inseminated. Using it up front can save 10 to 12 days of feed.                    |
| 3. | Make sure all heifers are inseminated. | Eazi-Breed <sup>™</sup> CIDR <sup>®</sup> should be used for timed breeding on heifers not inseminated during their first 28 days in the breeding pen. This will ensure all heifers are inseminated within 36 days of arrival into the AI pen. |
| 4. | Routine<br>pregnancy checks.           | Pregnancy diagnosis must be conducted as routinely as heifers are moved to the breeding pen to identify pregnant females and move them out, making room for new heifers. All pregnancies should be reconfirmed at 70 to 90 days carried calf.  |
| 5. | Re-enroll<br>open heifers.             | Any heifers that aren't bred should be immediately submitted to a timed breeding program with LUTALYSE or Eazi-Breed CIDR.   |

| Feedi | Feeding high plane of nutrition to reach growth goals |                        |                        | Breeding and pregnancy check |            |  |
|-------|---|------------------------|------------------------|------------------------------|------------|--|
|       | 375 to 400 days VWP                                   | 10 to 12 o             | days                   | 12 to 22 months              |            |  |
| Birth |   | 1                      | t                      |                              | Freshening |  |
|       |   | Administer<br>LUTALYSE | Administer<br>LUTALYSE |                              |            |  |

Managing heifer reproduction as intensely as the lactating herd can pay real dividends. Research has found that administering LUTALYSE on the day heifers are moved to the breeding pen, and then again 14 days later for animals not yet inseminated, can improve breeding success.<sup>5</sup> The incremental costs are minimal compared with the benefits calving heifers younger than 24 months of age can have on a dairy's bottom line.

**Important Safety Information:** Aseptic technique should be used to reduce the possibility of post-injection bacterial infections. Do not administer in pregnant animals unless cessation of pregnancy is desired. Not for intravenous administration. Women of childbearing age and persons with respiratory problems should exercise extreme caution when handling this product.

## Keys to great heifer reproduction.

| Move heifers to breeding pen when they reach size goals   |                 |               |       |        |        |  |  |  |  |
|---|-----------------|---------------|-------|--------|--------|--|--|--|--|
| <ul> <li>Heifers are ready to move when they reach 55 percent of mature size</li> <li>For a Holstein heifer, this is 800 to 850 pounds of body weight and 49 to 51 inches of wither height</li> </ul> |                 |               |       |        |        |  |  |  |  |
|   | Weight          | Height        | -     | Weight | Height |  |  |  |  |
| Current Size Upon Entry:  |                 |               | Goal: |        |        |  |  |  |  |
|   |                 |               | ·     |        |        |  |  |  |  |
| Reduce days to first insemination with LUTALYSE <sup>®</sup> (dinoprost tromethamine) Sterile Solution  |                 |               |       |        |        |  |  |  |  |
| • Target between 375 and 400 days   | 5               |               |       |        |        |  |  |  |  |
| Current age at first  |                 |               | Goal: |        |        |  |  |  |  |
|   |                 |               |       |        |        |  |  |  |  |
| Identify open heifers and rebreed   |                 |               |       |        |        |  |  |  |  |
| • All heifers should be confirmed p   | regnant by 15 r | months of age |       |        |        |  |  |  |  |
| Current average age   | at conception:  |               |       | Goal:  |        |  |  |  |  |
|   |                 |               |       |        |        |  |  |  |  |
| Monitor appropriate metrics   |                 |               |       |        |        |  |  |  |  |
| Current p   | regnancy rate:  |               |       | Goal:  |        |  |  |  |  |
| Current heat of   | detection rate: |               |       | Goal:  |        |  |  |  |  |
| Current co  | onception rate: |               |       | Goal:  |        |  |  |  |  |
|   |                 |               |       |        |        |  |  |  |  |

### Pay attention to management details

- Health of heifers
- Clean pens and corrals
- Sound vaccination program

- Efficiency of lock-ups
- Proper nutrition and feed bunk management

<sup>1</sup> Stuttgen S, Kohlman T, Hoffman P, Zwald A. There's nothing equal when raising heifers. Hoard's Dairyman 2008:87.

<sup>2</sup> Dairy 2007 Part II: Changes in the U.S. Dairy Cattle Industry, 1991-2007. National Animal Health Monitoring Service, U.S. Department of

Agriculture. Available at: http://nahms.aphis.usda.gov/dairy/index.htm. Accessed May 12, 2010.

- <sup>3</sup> Lormore M. Earlier first calving makes money. Northeast Dairy Business 2005:49-60.
- <sup>4</sup> Lormore M. The case for a quality dairy replacement program. Proceedings. NRAES Dairy Calves and Heifers: Integrating Biology and Management Conference, 2005.

<sup>5</sup> Stevenson JL, Rodrigues JA, Braga FA, Bitente S, Dalton JC, Santos JEP, Chebel RC. Effect of breeding protocols and reproductive tract score on reproductive performance of dairy heifers and economic outcomes of breeding programs. J Dairy Sci 2008;91:3424-3438.

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#### DAIRY WELLNESS MAKES A DIFFERENCE™



#### **LUTALYSE®** dinoprost tromethamine injection Sterile Solution

Caution: Federal 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 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.

#### 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, 16.5 mg added as preservative. When necessary, DH was adjusted with sodium hydroxide and/or hydrocholric acid. Dinoprost tromethamine is a white or slightly off-white crystalline powder that is readily soluble in water at room temperature in concentrations to the state of the state at least 200 mg/mL.

Cherreral Biologic Activity: Prostaglandins occur in nearly all mammalian tissues. Prostaglandins, especially PGE's and PGF's, 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 PGF2a, have been shown to 1) increase at inthe uterus and blood to levels similar to levels achieved by exogenous administration which elicited luteolysis, 2) be capable 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 pluitary tropic hormones. Data suggest prostaglandins, especially PGE's and PGF's, may be involved in the process of ovulation and gamete transport. Also PGF2a has been reported to cause increase in blood pressure, processericition, and smooth muscle stimulation in cartain species. bronchoconstriction, and smooth muscle stimulation in certain species.

#### METABOLISM

METABOLISM A number of metabolism studies have been done in laboratory animals. The metabolism of tritium labeled dinoprost (3H PGF2 alpha) in the rat and in the monkey was similar. Although quantitative differences were observed, qualitatively similar metabolites were produced. A study demonstrated that equimolar doese of 3H PGF2 alpha Tham and 3H PGF2 alpha The 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 3H PGF2 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 3H PGF2 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, excretory, binding or other systems need be established by the body to metabolize injected dinoprost.

INDICATIONS AND USAGE
 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 ovulated 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 do not be injection, cattle should be bred at the usual time relative to estrus. With the single injection, cattle should be bred at the usual time relative to estrus.

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 5 mL LUTALYSE (25 mg PGF2α) 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: 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:

- 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 as this has a direct effect on conception and the initiation of estrus in heifers or return of estrous cycles in cows following; 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;

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;
f. Semen must be inseminated property.
A successful breeding program can employ LUTALYSE effectively, but a poorly managed breeding program will continue to be poor when LUTALYSE is employed unless other management deficiencies are remedied first. Cattle expressing estrus following LUTALYSE are receptive to breeding by a bull. Using bulls to breed large numbers of cattle in heat following LUTALYSE are receptive to breeding by a bull. Using bulls to breed large numbers of cattle in heat following LUTALYSE is sufficient of Pyometra (chronic endometritis) in Cattle. Inject a dose of 5 mL UTALYSE (25 mg PGFza) intramuscularly. Its totiles conducted with LUTALYSE, pyometra was defined as presence of a corpus luteum in the ovary and uterine horns containing fluid but not a conceptus based on palpation per rectum at 14 and 28 days. Most cattle hard ecovered in response to LUTALYSE is indicated of the lutar hand in a tertur on the uterine horn size to 40mm reless based on palpation per rectum at 14 and 28 days. Most cattle hard content Non-Lactating Cattle. LUTALYSE is indicated for its abortilacient effect in feedlot and other non-Lactating Cattle. LUTALYSE is indicated for its abortilacient effect in feedlots. The percent of pregnant cattle were palpated per rectum for pregnancy in six feedlots. The percent of pregnant cattle were lass than 150 days of gestation. Inject a dose of 34, 80% or more of the pregnant cattle were lass than 150 days of gestation. rates following injection of LUTALYSE increasing doses up to about 25 m, As examples, the abortion rates following injection of LUTALYSE is for ads of gestation.
Swime: For intramuscular use for parturition induction in while. LUTALYSE Ster

1. Controlling Time of Estrus of Estrous Cycling Mares: Mares treated with LUTALYSE 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 Marses: In extended diestrus there is failure to exhibit regular estrous cycles which is different from true anestrus. Many mares described as an estrus during the breeding season have serum progesterone levels

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 letal 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 usually results in regression of the corpus luteum followed by estrus and/or oxulation. In one study with 122 Standardbred and Thoroughbred mares in clinical anestrus for an average of 58 days and treated 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, 59% were pregnant following an average of 1.4 services during that estrus. Treatment of "anestrous" mares which abort subsequent to 36 days of pregnancy may not result in return to estrus due to presence of functional endometrial cuos.

due to presence of functional endometrial cups.

#### WARNINGS

WARNINGS User Safety: 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 may be unaware of their pregnancies. Dinoprost tromethamine is readily absorbed through the skin and can cause abortion. Accidental spillage on the skin should be washed of immediately with soap and water. Residue Warnings: No milk discard or preslaughter drug withdrawal period is required for labeled uses in a 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 clostridial infections associated with injection of LUTALYSE have been reported. In rare instances, such infections have resulted in death. Aggressive antibiotic therapy should be employed at the first sign of infection at the injection site whether localized or diffuse.

#### PRECAUTIONS

- PhecAdUIONS Do not administer intravenously (I.V.) as this route may potentiate adverse reactions. 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. As with all parenteral products careful aseptic techniques should be used to decrease the possibility of post-injection bacterial infections. The vial stopper should be cleaned and disinfected prior to needle entry. Only sterile needles should be used and the same needle should not be used more than once. Nonsteroidal anti-inflammatory drugs may inhibit prostaglandin synthesis; therefore this class of drugs should not be administered concurrently.

Nonsteroidal anti-inflammatory drugs may inhibit prostaglandin synthesis; therefore this class of drugs should not be
administered concurrently.
 Cattle: Do not administer to pregnant cattle, unless abortion is desired. Cattle administered a progestin would be
expected to have a reduced response to LUTALYSE Sterile Solution.
 Swine: Do not administer to sows and/or gilts prior to 3 days of normal predicted farrowing as an increased number
of stilbirths and postnatal mortality may result.
 Mares: LUTALYSE Sterile Solution is ineflective 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.

#### ADVERSE REACTIONS

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 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 respiration 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 Sterile Solution was reported but was not confirmed. To report adverse reactions call Pfizer Animal Health at 1-800-366-5288.

#### DOSAGE AND ADMINISTRATION

As with any multi-dose vial, practice aseptic techniques in withdrawing each dose. Adequately clean and disinfect the vial stopper prior to entry with a sterile needle and syringe. No vial closure should be entered more than 20 times. **Cattle:** LUTALYSE Sterile Solution is supplied at a concentration of 5 mg dinoprost per mL. LUTALYSE is luteolytic in cattle at 25 mg (5 mL) administered intramuscularly. Swine: LUTALYSE Sterile Solution will induce parturition in swine at 10 mg (2 mL) when injected intramuscularly

Mares

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 anestrous mares will not express estrus but will develop a follicle which will ovulate. These mares may become pregnant if inseminated at the appropriate time relative to rupture of the follicle.
5. Breed mares in estrus in a manner consistent with normal management.

#### SAFETY AND TOXICITY

SAFETY AND TOXICITY Laboratory Animals: Dinoprost was non-teratogenic in rats when administered orally at 1.25, 3.2, 10.0 and 20.0 mg/ kg/day from day 6th-15th of gestation or when administered subcutaneously at 0.5 and 1.0 mg/kg/day on gestation days 6, 7 and 8 or 9, 10 and 11 or 12, 13 and 14. Dinoprost was non-teratogenic in the rabbit when administered either subcutaneously at doses of 0.5 and 1.0 mg/kg/day on gestation days 6, 7 and 8 or 9, 10 and 11 or 12, 13 and 14.0 15, 16 and 17 or orally at doses of 0.01, 0.1 and 1.0 mg/kg/day on days 6-18 or 5.0 mg/kg/day or 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 per 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 PGF2 per kg body weight for 14 days.

changes were not observed in monkeys similarly administered LUTALYSE Sterile Solution. Tweel, sour howes, source and source and the source of the source of

Induction of partimiter of abortion with any exogenous composition may precipitate oystocia, teta death, retained placenta and/or metritis, especially at latter stages of gestation. Swine: In pigs, evaluation was made of clinical observations, food consumption, clinical pathologic determinations, body weight changes, urinalysis, organ weights, and gross and microscopic observations following treatment with single doses of 10, 30, 50 and 100 mg dinoprost administered intramuscularly. The results indicated no treatment that were deteletions 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 old), at the rates of 0, 100, 200, 400, and 800 mg per mare per day for 8 days. Route of administration for each dose group was both intramuscularly (2 mares) and subcutaneously (2 mares). Changes were detected in all treated groups for clinical (reduced sensitivity to pain; locomotor incoordination; hypergastromotility; sweating; hyperthermia; labored cesinophils; increased hemoglobin, hematocrit, and erythrocytes) measurements. The effects in the 100 mg dose, and to a lesser extent, the 220 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 gastrointestinal tract caused a protracted diarrhea, slight electrolyte imbalance (decreased sodium and potassium), dehydration, gastrointestinal tract caused a contracted. Other measurements evaluated in the study remained within normal limits. No mortality occurred in any of the groups. No apparent differences were observed between the intramuscular and subcutaneous not day, therefore, LUTALYSE was demonstrated to have a wide margin of 30.4, 0.20, 50, 0.0, 0.75, 1.0, 1.5, 2.0, 3.0, 4.0, 5.0, and 6.0 hr. after injection. Neither heat rate nor respiration rates were significantly attered (P > 0.05) when compared to contheroprary control values. Sweating was measeared of 0 of 9,

HOW SUPPLIED LUTALYSE Sterile Solution is available in 30 and 100 mL vials.

STORAGE CONDITIONS Store at controlled room temperature 20° to 25° C (68° to 77° F). Protect from freezing

Restricted Drug (California), Use Only As Directed

NADA #108-901, Approved by FDA U.S. Patent No. 6,187,818

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