

Dairy profitability requires good fertility management.

- A missed heat cycle can cost as much as \$29¹
- A missed pregnancy costs an average of \$450²
- Poor reproductive performance and extended lactations decrease from the producer's bottom line

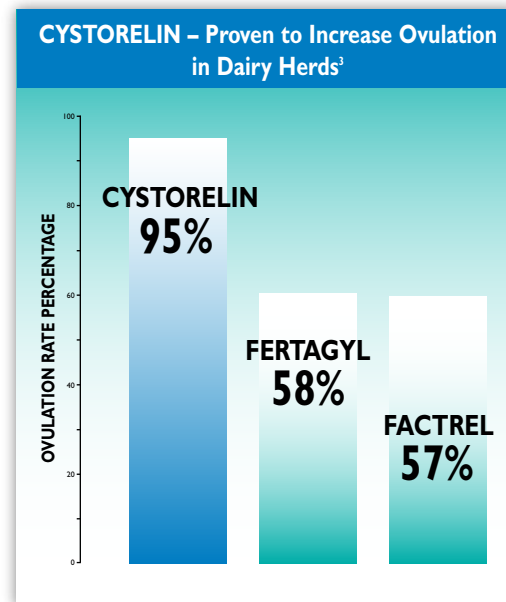
Don't miss an opportunity like this.

With \$450 on the line, you need a product that's proven to help dairy herds conceive and calve on schedule. That product is CYSTORELIN[®] (gonadorelin diacetate tetrahydrate).

Compare CYSTORELIN with other GnRH products.

Research shows that CYSTORELIN is more effective than other GnRH products in initiating the release of endogenous luteinizing hormone (LH) to cause ovulation and luteinization.³ In a study comparing three gonadorelin products, results showed:

- **CYSTORELIN induced ovulation in 95% of dairy cows** while FERTAGYL[®] (gonadorelin) induced ovulation in 58% and FACTREL[®] (gonadorelin hydrochloride) induced ovulation in 57% ($P < 0.02$)³
- CYSTORELIN induced the highest mean and the highest peak LH response³
- CYSTORELIN consistently induced sufficient LH release to cause the ovulation of the dominant follicle³



CYSTORELIN
is the #1 selling
brand of GnRH
in the U.S.⁴



Original.

Reproduction.



CYSTORELIN[®]. Millions of calves and counting.



CYSTORELIN. The trusted and effective GnRH.

- Used to treat ovarian follicular cysts, thereby activating the process leading to estrus
- Initiates the release of endogenous luteinizing hormone (LH) to cause ovulation and luteinization
- The first GnRH approved by the FDA for cattle

CYSTORELIN is easy to use.

- Intramuscular (IM) or intravenous administration
- 2 mL dose
- No milk withholding
- As with other GnRH products, refrigerate sealed and opened bottles to maximize product stability



Each 10 mL bottle contains five doses.
A case includes 20 bottles, or 100 doses.

CYSTORELIN®

(gonadorelin diacetate tetrahydrate)

FOR INJECTION

For the treatment of cystic ovaries in cattle.

DESCRIPTION:

CYSTORELIN is a sterile solution containing 50 micrograms of gonadorelin (GnRH) diacetate tetrahydrate per milliliter suitable for intramuscular or intravenous administration. Gonadorelin is a decapeptide composed of the sequence of amino acids –

5-oxoPro-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH₂

a molecular weight of 1182.32 and empirical formula C₄₂H₆₄N₁₀O₁₀. The diacetate tetrahydrate ester has a molecular weight of 1374.48 and empirical formula of C₄₈H₇₆N₁₀O₁₂.

Gonadorelin is the hypothalamic releasing factor responsible for the release of gonadotropins (e.g. LH, FSH) from the anterior pituitary. Synthetic gonadorelin is physiologically and chemically identical to the endogenous bovine hypothalamic releasing factor.

PHARMACOLOGY AND TOXICOLOGY:

Endogenous gonadorelin is synthesized and/or released from the hypothalamus during various stages of the bovine estrus cycle, following appropriate neurogenic stimuli. It passes via the hypophyseal portal vessels to the anterior pituitary, to effect the release of gonadotropins (e.g. LH, FSH). Synthetic gonadorelin administered intravenously or intramuscularly also causes the release of endogenous LH or FSH from the anterior pituitary.

Gonadorelin diacetate tetrahydrate has been shown to be safe. The LD₅₀ for mice and rats is greater than 60 mg/kg, and for dogs greater than 600 mcg/kg, respectively. No untoward effects were

noted among rats or dogs administered 120 mcg/kg/day or 72 mcg/kg/day intravenously for 15 days.

It has no adverse effects on heart rate, blood pressure or EKG to unanesthetized dogs at 60 mcg/kg. In anesthetized dogs, it did not produce depression of myocardial or system hemodynamics or adversely affect coronary oxygen supply or myocardial oxygen requirements.

The intravenous administration of 60 mcg/kg/day of gonadorelin diacetate tetrahydrate to pregnant rats and rabbits during organogenesis did not cause embryotoxic or teratogenic effects.

The intramuscular administration of 1000 mcg to normally cycling dairy cattle had no effect on hematology or blood chemistry.

Further, CYSTORELIN does not cause irritation at the site of intramuscular administration in dogs. The dosage administered was 72 mcg/kg/day for seven (7) days.

INDICATIONS AND DOSAGE:

CYSTORELIN (gonadorelin diacetate tetrahydrate) is indicated for the treatment of ovarian follicular cysts in dairy cattle. Ovarian cysts are non-ovulated follicles with incomplete luteinization which result in nymphomania or irregular estrus.

Historically, cystic ovaries have responded to an exogenous source of luteinizing hormone (LH) such as human chorionic gonadotropin.

CYSTORELIN initiates release of endogenous LH to cause ovulation and luteinization.

The recommended intravenous or intramuscular dosage of CYSTORELIN is 100 mcg/cow.

Each mL of CYSTORELIN contains:

Gonadorelin diacetate tetrahydrate.....	50 mcg
Benzyl Alcohol.....	9 mg
Sodium Chloride.....	7.47 mg
Water for Injection, U.S.P.....	q.s.

pH adjusted with potassium phosphate (monobasic and dibasic)

PRECAUTIONS:

Not for use in humans.

Keep this and all drugs out of reach of children.

The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information.

To report adverse effects in users, to obtain an MSDS or for assistance, call 1-888-637-4251.

KEEP REFRIGERATED: 2° – 8°C (36° – 46°F)

CAUTION: Federal (U.S.A.) law restricts this drug to use by, or on the order of, a licensed veterinarian.

HOW SUPPLIED:

CYSTORELIN is available in a concentration of 50 mcg/mL pH adjusted with potassium phosphate (monobasic and dibasic). CYSTORELIN is supplied in multi-dose vials containing 10 mL of sterile solution.

Write for additional information about CYSTORELIN.

NADA 098-379, Approved by FDA
Marketed by: Merial Limited, Duluth, GA 30096



CYSTORELIN®
(gonadorelin diacetate tetrahydrate)

¹ Meadows, C. A spreadsheet-based model demonstrating the nonuniform economic effects of varying reproductive performance in Ohio dairy herds. *J Dairy Sci.* 2005;88:1244–1254.

² Fricke, PM, et al. Pregnant vs. open: Getting cows pregnant and the money it makes. *Proceedings, Western Dairy Management Conference.* 2005:49-62.

³ Martinez MF, Mapletoft RJ, Kastelic JP, Carruthers T. The effects of 3 gonadorelin products on luteinizing hormone release, ovulation and follicular wave emergence in cattle. *Canadian Vet J.* 2003;44:125-131.

⁴ Data on file.



www.merial.com
1-888-637-4251

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