CYSTORELIN- gonadorelin injection, solution
Boehringer Ingelheim Animal Health USA Inc.

CYSTORELIN®
(gonadorelin)
50 mcg/mL gonadorelin diacetate tetrahydrate Injectable Solution

For treatment of cystic ovaries in dairy cattle

For use with cloprostenol sodium to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows and beef cows.

CAUTION:

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:

CYSTORELIN® is a sterile solution containing 43 mcg/mL of gonadorelin (GnRH) as 50 mcg/mL gonadorelin diacetate tetrahydrate suitable for intramuscular or intravenous administration according to the indication. Gonadorelin is a decapeptide composed of the sequence of amino acids—

5-oxoPro-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH_2—

a molecular weight of 1182.32 and empirical formula $C_{55}H_{75}N_{17}O_{13}$. The diacetate tetrahydrate ester has a molecular weight of 1374.48 and empirical formula $C_{59}H_{91}N_{17}O_{21}$.

Each mL of CYSTORELIN contains:

Gonadorelin diacetate tetrahydrate (equivalent to 43 mcg gonadorelin) 50 mcg

Benzyl Alcohol 9 mg

Sodium Chloride 7.47 mg

Water for Injection q.s.

pH adjusted with potassium phosphate (monobasic and dibasic).

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

INDICATIONS FOR USE:

Cystic Ovaries

CYSTORELIN 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 LH such as human chorionic gonadotropin. CYSTORELIN initiates release of endogenous LH to cause ovulation and luteinization.

Reproductive Synchrony

CYSTORELIN is indicated for use with cloprostenol sodium to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows and beef cows.

DOSAGE AND ADMINISTRATION:

Cystic Ovaries

The intravenous or intramuscular dosage of CYSTORELIN is 100 mcg gonadorelin diacetate tetrahydrate (2 mL) per cow.

Reproductive Synchrony

The intramuscular dosage of CYSTORELIN is 100 mcg gonadorelin diacetate tetrahydrate (2 mL) per cow, used in reproductive synchrony programs similar to the following:

1. Administer the first CYSTORELIN injection (2 mL) at Time 0.

2. Administer 500 mcg cloprostenol (as cloprostenol sodium) by intramuscular injection 6 to 8 days after the first CYSTORELIN injection.

3. Administer the second CYSTORELIN injection (2 mL) 30 to 72 hours after the cloprostenol sodium injection.

4. Perform FTAI 0 to 24 hours after the second CYSTORELIN injection, or inseminate cows on detected estrus using standard herd practices.

WARNINGS AND PRECAUTIONS:

Not for use in humans.

Keep out of reach of children.

WITHDRAWAL PERIODS:

No withdrawal period or milk discard time is required when used according to the labeling.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or www.fda.gov/reportanimalae.

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 LD_{50} for mice and rats is greater than 60 mg/kg, and for dogs, greater than 600 mcg/kg, respectively. No adverse effects were noted among rats or dogs administered 120 mcg/kg/day or 72 mcg/kg/day intravenously for 15 days.

It had 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.

Further, CYSTORELIN did not cause irritation at the site of intramuscular administration in dogs with a dose of 72 mcg/kg/day administered for seven (7) days.

TARGET ANIMAL SAFETY:

In addition to the animal safety information presented in the PHARMACOLOGY AND TOXICOLOGY section, the safety of CYSTORELIN was established through the review and evaluation of the extensive published literature available for the use of gonadorelin-containing products.

The intramuscular administration of 1000 mcg gonadorelin diacetate tetrahydrate on five (5) consecutive days to normally cycling dairy cattle had no effect on hematology or clinical chemistries.

In field studies evaluating the effectiveness of CYSTORELIN for the treatment of ovarian follicular cysts, the incidence of health abnormalities was not significantly greater in cows administered CYSTORELIN than cows administered a placebo injection.

The target animal safety of, and injection site reactions to, gonadorelin when used with cloprostenol sodium were evaluated during the conduct of effectiveness field studies. The incidence of health abnormalities was not significantly greater in cows administered gonadorelin than cows administered a placebo injection.

EFFECTIVENESS:

The use of CYSTORELIN for treatment of ovarian follicular cysts in dairy cattle was demonstrated to be effective with a treatment dose of 100 mcg gonadorelin diacetate tetrahydrate.

The effectiveness of gonadorelin for use with cloprostenol sodium to synchronize estrous cycles to allow for FTAI in lactating dairy cows was demonstrated in a field study at 10 different locations in the U.S. Four of the locations represented conditions that would typically cause heat stress in lactating cows. A total of 1607 healthy, non-pregnant, primiparous or multiparous lactating dairy cows within 40-150 days postpartum were enrolled in the study. A total of 805 cows were administered gonadorelin (1 mL; 100 mcg gonadorelin as the acetate salt) and 802 cows were administered an equivalent volume of water for injection as an intramuscular injection twice in the following regimen:

Day 0: 100 mcg gonadorelin (as the acetate salt) or sterile water for injection

Day 7: 500 mcg cloprostenol (as cloprostenol sodium)

Day 9: 100 mcg gonadorelin (as the acetate salt) or sterile water for injection

Fixed time AI was performed on Day 10, approximately 11 - 31 hours after the Day 9 injection. Cows were evaluated for pregnancy on Day 45 ± 5 days by trans-rectal ultrasound or rectal palpation. Pregnancy rate to FTAI was significantly higher ($P < 0.0001$) in cows treated with gonadorelin (33.4%) than the pregnancy rate to FTAI in cows treated with water (13.6%). The environmental condition (heat stress or not heat stress) did not affect the conclusion of effectiveness.

The effectiveness of gonadorelin for use with cloprostenol sodium to synchronize estrous cycles to allow for FTAI in beef cows was demonstrated in a field study at 10 different locations in the U.S. A total of 706 healthy, non-pregnant, primiparous or multiparous beef cows within 40-150 days postpartum were enrolled in the study. A total of 364 cows were administered gonadorelin (1 mL; 100 mcg gonadorelin as the acetate salt) and 342 cows were administered an equivalent volume of water for injection as an intramuscular injection twice in the following regimen:

Day 0: 100 mcg gonadorelin (as the acetate salt) or sterile water for injection

Day 7: 500 mcg cloprostenol (as cloprostenol sodium)

Day 9: 100 mcg gonadorelin (as the acetate salt) or sterile water for injection

Fixed time AI was performed immediately after the Day 9 injection. Cows were evaluated for pregnancy on Day 55 ± 5 days by trans-rectal ultrasound. Pregnancy rate to FTAI was significantly higher ($P = 0.0006$) in cows treated with gonadorelin (21.7%) than the pregnancy rate to FTAI in cows treated with water (7.4%).

The effectiveness of a 2-mL dose of CYSTORELIN delivering 100 mcg gonadorelin diacetate tetrahydrate (86 mcg gonadorelin) for use with cloprostenol sodium to synchronize estrous cycles to allow for FTAI in lactating dairy cows and beef cows was also demonstrated through references to scientific literature.

HOW SUPPLIED:

CYSTORELIN is available in a concentration of 50 mcg/mL gonadorelin diacetate tetrahydrate (43 mcg/mL gonadorelin) pH adjusted with potassium phosphate (monobasic and dibasic).

CYSTORELIN is supplied in multi-dose vials containing 10 mL, 30 mL, 50 mL, and 100 mL of sterile solution.

STORAGE, HANDLING, AND DISPOSAL:

Store at or below 77°F (25°C). Brief excursions to 86°F (30°C) are permitted. Use within 6 months of first puncture.

Principal Display Panel – 50 mL Bottle Carton

CYSTORELIN®
(gonadorelin)

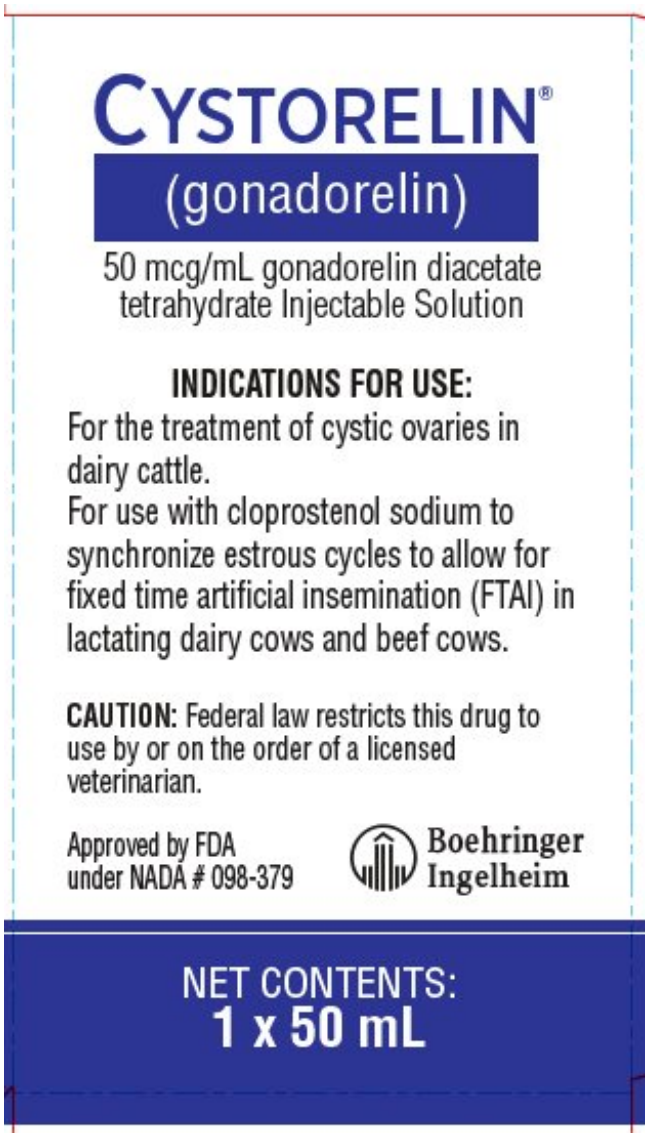
(50 mcg/mL) gonadorelin diacetate tetrahydrate Injectable Solution

INDICATIONS FOR USE:

For the treatment of cystic ovaries in dairy cattle. For use with cloprostenol sodium to synchronize estrous cycles to allow for fixed-time artificial insemination (FTAI) in lactating dairy and beef cows.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Approved by FDA under NADA # 098-379



CYSTORELIN
gonadorelin injection, solution

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:0010-8283
Route of Administration	INTRAVENOUS, INTRAMUSCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
GONADORELIN DIACETATE TETRAHYDRATE (UNII: L8CRY8PWF2) (GONADORELIN - UNII:9O7312W37G)	GONADORELIN DIACETATE TETRAHYDRATE	50 ug in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BENZYL ALCOHOL (UNII: LKG8494WBH)	9 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	7.47 mg in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0010-8283-01	1 in 1 CARTON		
1		10 mL in 1 BOTTLE, GLASS		
2	NDC:0010-8283-03	10 in 1 CARTON		
2	NDC:0010-8283-02	30 mL in 1 BOTTLE, GLASS		
3	NDC:0010-8283-04	50 mL in 1 BOTTLE, GLASS		
4	NDC:0010-8283-05	100 mL in 1 BOTTLE, GLASS		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA098379	02/19/2020	

Labeler - Boehringer Ingelheim Animal Health USA Inc. (007134091)

Revised: 8/2025 Boehringer Ingelheim Animal Health USA Inc.