FERTAGYL- gonadorelin injection
Merck Sharp & Dohme Corp.

FERTAGYL®
(GONADORELIN)
43 mcg/mL gonadorelin Sterile Solution

ANADA 200-134 Approved by FDA
159942 R1

FOR THE TREATMENT OF CYSTIC OVARIES IN DAIRY CATTLE
FOR USE WITH ESTRUMATE (CLOPROSTENOL INJECTION) TO SYNCHRONIZE ESTROUS CYCLES
TO ALLOW FOR FIXED TIME ARTIFICIAL INSEMINATION (FTAI) IN LACTATING DAIRY COWS

CAUTION

FEDERAL LAW RESTRICTS THIS DRUG TO USE BY OR ON THE ORDER OF A LICENSED VETERINARIAN.

DESCRIPTION

Fertagyl is a sterile solution containing 43 mcg gonadorelin (GnRH; as gonadorelin acetate) per milliliter 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

with a molecular weight of 1182.32 and empirical formula $C_{55}H_{75}N_{17}O_{13}$.

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 by and/or released from the hypothalamus during various stages of the bovine estrous 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 intramuscularly or intravenously also causes the release of endogenous LH and FSH from the anterior pituitary. Gonadorelin acetate 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 untoward effects were noted among rats or dogs administered 120 mcg/kg/day intramuscularly or 72 mcg/kg/day intravenously for 15 days.

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

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

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

Further, gonadorelin acetate did not cause irritation at the site of intramuscular administration in dogs. The dosage administered was 72 mcg/kg/day for 7 days.

INDICATION AND DOSAGE

Cystic Ovaries

Fertagyl (gonadorelin) 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.

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

The recommended intramuscular or intravenous dosage of Fertagyl is 86 mcg gonadorelin (2 mL)/cow.

DO NOT PUNCTURE STOPPER MORE THAN 10 TIMES

Reproductive Synchrony

Fertagyl (gonadorelin) is indicated for use with Estrumate (cloprostenol injection) to synchronize estrous cycles to allow for fixed-time artificial insemination (FTAI) in lactating dairy cows.

The recommended intramuscular dosage of Fertagyl is 86 mcg gonadorelin (2 mL) per cow, used in reproductive synchrony programs similar to the following:

- Administer the first Fertagyl injection (2 mL) on Day 0
- Administer 2mL of Estrumate (500 mcg cloprostenol, as cloprostenol sodium) by intramuscular injection 6-8 days after the first Fertagyl injection
- Administer the second Fertagyl injection (2mL) 30 to 72 hours after the Estrumate injection
- Perform FTAI 8 to 24 hours after the second Fertagyl injection, or inseminate cows on detected estrus using standard herd practices.

TARGET ANIMAL SAFETY

In addition to the target animal information presented in the section addressing pharmacology and toxicology, target animal safety of, and injection site reactions to, Fertagyl (gonadorelin) when used with Estrumate (cloprostenol injection) were evaluated during the conduct of the effectiveness field studies. The incidence of health abnormalities was not significantly greater in cows administered with Fertagyl than cows administered a placebo injection.

EFFECTIVENESS

The effectiveness of Fertagyl (gonadorelin) for use with Estrumate (cloprostenol injection) to synchronize estrous cycles to allow for FTAI in lactating dairy cows was demonstrated in a field study at six different locations in the U.S. A total of 758 healthy, non-pregnant, primiparous or multiparous lactating dairy cows within 50-120 days postpartum were enrolled in the study. A total of 377 cows were administered Fertagyl (2mL; 86 mcg gonadorelin as the acetate salt) and 381 cows were administered an equal volume of saline as an intramuscular injection twice in the following regimen:

Day 0: 2 mL Fertagyl or saline
Day 7: 2 mL Estrumate (cloprostenol injection)
Day 9: 2 mL Fertagyl or saline

Fixed time AI was performed on Day 10, 16 ± 8 hours after the Day 9 injection. Cows were evaluated for pregnancy on 45 ± 5 days by trans-rectal ultrasound or rectal palpation. Pregnancy rate to FTAI was significantly higher (P=0.0051) in cows treated with Fertagyl (33.4%) than the pregnancy rate to FTAI to cows treated with saline (17.8%).

Each mL of Fertagyl contains:	
Gonadorelin (as gonadorelin acetate)	43 mcg
Benzyl Alcohol	9 mg

Sodium Chloride	7.47 mg
Water for Injection, USP	q.s.

pH adjusted with sodium phosphate (monobasic and dibasic).

STORAGE CONDITIONS: Keep refrigerated: 2°-8°C (36°-46°F).

USE WITHIN 28 DAYS OF FIRST USE

PRECAUTIONS

FOR ANIMAL USE ONLY. NOT FOR HUMAN USE. KEEP OUT OF THE REACH OF CHILDREN.

The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. To report adverse effects in users to obtain a MSDS or for assistance call 1-800-211-3573

HOW SUPPLIED

Fertagyl is a sterile solution containing 43 mcg gonadorelin (GnRH; as gonadorelin acetate) per milliliter suitable for intramuscular or intravenous administration according to the indication.

Fertagyl is supplied in multidose vials containing 20 mL and 100 mL of sterile solution.

Manufactured for:
INTERVET INC. (d/b/a Merck Animal Health)
Madison, NJ 07940
By: INTERVET INTERNATIONAL GmbH
Unterschleissheim – Germany

PRINCIPAL DISPLAY PANEL - 20 mL Vial Carton

MERCK
Animal Health

20 mL

fertagyl®
(gonadorelin)

43 mcg/mL gonadorelin Sterile Solution

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

For animal use only. Not for human use. Keep out of reach of children.

ANADA 200-134,
Approved by FDA

Net Contents:
20 mL/10 doses

MERCK
Animal Health

FERTAGYL

gonadorelin injection

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:57926-477
Route of Administration	INTRAMUSCULAR, INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
GONADORELIN (UNII: 9O7312W37G) (GONADORELIN - UNII:9O7312W37G)	GONADORELIN	43 ug in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
Sodium Chloride (UNII: 451W47IQ8X)	
Sodium Phosphate, Monobasic, Dihydrate (UNII: 5QWK665956)	
Benzyl Alcohol (UNII: LKG8494WBH)	
water (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:57926-477-07	1 in 1 CARTON		
1		20 mL in 1 VIAL, MULTI-DOSE		
2	NDC:57926-477-67	1 in 1 CARTON		
2		100 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200134	06/17/1996	

Labeler - Merck Sharp & Dohme Corp. (001317601)

Establishment

Name	Address	ID/FEI	Business Operations
Intervet International GMBH		328855635	MANUFACTURE

Establishment

Name	Address	ID/FEI	Business Operations
Aspen Oss B.V.		491017488	API MANUFACTURE

Revised: 8/2015 Merck Sharp & Dohme Corp.