Product Monograph Information

SOLVET

Telephone: 1-403-456-2245
Toll-Free: 1-877-456-2755
Fax: 1-403-271-2920
Website: www.solvet.ca
Email: info@solvet.ca

GONAbreed®

Gonadorelin acetate injection
Veterinary Use Only, Sterile
DIN: 02496763

Equivalent to 100 µg gonadorelin/mL

This treatment applies to the following species:
• Beef Cattle
• Dairy Cattle

Description: Gonadorelin is a decapeptide composed of the sequence of amino acids: 5-oxoPro-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH_2. It has a molecular weight of 1,182.32 g/mol and empirical formula of $C_{55}H_{75}N_{17}O_{13}$. The molecular formula of its acetate is $C_{55}H_{75}N_{17}O_{13} \cdot C_2H_4O_2$ with a molecular weight of 1,242.3 g/mol.

Ingredients - Each mL contains:

Active ingredient: Gonadorelin (as gonadorelin acetate): 100 µg
Preservative: Benzyl alcohol: 10 mg
Non-medicinal ingredients:
Sodium chloride: 7.47 mg
Sodium phosphate monobasic: 8.3 mg
Sodium phosphate dibasic: 4.8 mg
Hydrochloric acid or sodium hydroxide for pH adjustment
Water for injection: q.s. to 1 mL

Indications: GONAbreed is a hormone indicated for use with cloprostenol sodium injectable solution to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows and beef cows.

Dosage and Administration: Administer 100 µg (1 mL) of GONAbreed per cow intramuscularly following a reproductive synchrony program similar to the following:

- Administer the first GONAbreed injection (1 mL) at Time 0.
- Administer 500 µg cloprostenol (as cloprostenol sodium) by intramuscular injection 6 to 8 days after the first GONAbreed injection.
- Administer the second GONAbreed injection (1 mL) 30 to 72 hours after the cloprostenol sodium injection.
- Perform FTAI 0 to 24 hours after the second GONAbreed injection,or inseminate cows on detected estrus using standard herd practices.

Proper injection techniques including the usage of a proper gauge needle, and cleaning and sanitizing the injection site prior to administering the recommended dose should be followed. Tissue damage and trimming loss of injection site has not been assessed.

Warnings: No meat withdrawal period and no milk discard time are required when used according to the label. When handling this product, caution should be taken to avoid accidental self-injection or contact with the skin or mucous membranes. Keep out of reach of children. The Safety Data Sheet (SDS) contains more detailed occupational safety information. To obtain an SDS, for technical assistance, or to report a suspected adverse drug experience, contact Parnell at 1-800-88-PARNELL (1-800-887-2763).

Adverse Reactions:
Clostridial infections at the injection site and anaphylactic reactions have been very rarely reported following administration of this product. Treated animals should be closely observed post injection and appropriate therapy initiated as required.

Clinical Pharmacology:
GENERAL BIOLOGIC ACTIONS: Gonadorelin is the hypothalamic releasing factor responsible for the release of gonadotropins (i.e. luteinizing hormone (LH) and follicular stimulating hormone (FSH)) from the anterior pituitary. Synthetic gonadorelin is physiologically and chemically identical to the endogenous bovine hypothalamic releasing factor. Endogenous gonadorelin is synthesized and released by 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 (i.e., LH, FSH). Synthetic gonadorelin administered intramuscularly also causes the release of endogenous LH and FSH from the anterior pituitary.

TARGET ANIMAL SAFETY:
Sixteen non-pregnant lactating dairy cows were enrolled in a Target Animal safety trial, where eleven of the cows were randomly allocated to receive one intramuscular injection of 5 mL of GONAbreed (500 mcg gonadorelin acetate; 5X of the recommended label dose), and the remaining five cows each received a single dose of 5 mL of saline intramuscularly. Clinical assessment of general health and injection site observations were performed on study Days 0 - 11 by the study veterinarian and the producer. Blood samples were collected on study Days -7, 1, and 8 for hematology and chemistry testing. With the exception of one cow in the control group that had facial eczema, all other cows in both treatment groups had a normal clinical assessment, normal blood analyses and no observed injection site reactions.
Two field trials were conducted to assess the efficacy and safety in field conditions of GONAbreed, one in beef cattle and another in dairy cattle. Seven hundred and six (706) and 1,607 cows were enrolled in the beef cattle and dairy cattle studies, respectively. In both trials, animals were randomly allocated to either undergo treatment in a GPG program (GONAbreed-Prostaglandin-GONAbreed) or receive a placebo and prostaglandin alone (sterile water-Prostaglandin-sterile water).
In the beef cattle study, injection site reactions to GONAbreed or placebo were assessed daily from study Days 0 - 16 and then weekly until the end of the study and adverse events were reported throughout the course of the study. The percentage of animals with injection site reactions (3.5% and 2.6%) and the percentage of adverse events (3.7% and 4.4%) were comparable between treatment and control groups, respectively. Adverse events in both groups were limited to lameness, ocular lesions, and abscesses from previous injections. In one case, an abscess was reported 3 weeks after the last administration of GONAbreed; it is unclear whether it was associated with the test article. One cow in the control group died on study Day 57 and the cause of death was inconclusive.
In the dairy cattle study, injection site reactions to GONAbreed or placebo administered on study Day 0 were assessed seven days later by the study investigator or designated person. Herdsmen observed and reported injection site reactions and adverse events on a daily basis throughout the study. The percentage of animals with injection site reactions (3.5% and 4.6%) and the percentage of adverse events (4.2% and 3.4%) were comparable between the treatment and control groups, respectively, with the majority of adverse events being due to mastitis (74.4% and 87.5% for the treatment and control groups, respectively). Other adverse events included pneumonia, neck swelling, lameness, recumbency, and abdominal pain. Eight cows died/euthanized throughout the course of the study (5 in the treatment

group and 3 in the control group). Three of the cows in the treatment group were euthanized due to injuries, one died due to hemorrhagic bowel syndrome, and the other due to gastrointestinal illness and/or pneumonia. The cause of death for cows that died in the control group were injury, lymphosarcoma, and an undetermined cause.

Effectiveness:
DAIRY COWS: The effectiveness of GONAbreed for use with injectable 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. A total of 1,607 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 GONAbreed (1 mL; 100 µg gonadorelin as the acetate salt) and 802 cows were administered an equivalent volume of water as an intramuscular injection twice in the following regimen:

Day 0: 1 mL GONAbreed or sterile water for injection
Day 7: 500 µg cloprostenol, as cloprostenol sodium
Day 9: 1 mL GONAbreed or sterile water for injection

Fixed time AI was performed on Day 10, 11-31 hours after the Day 9 injection. Cows were evaluated for pregnancy on Day 45 ± 5 days by transrectal ultrasound or rectal palpation. Pregnancy rate to FTAI was significantly higher ($P<0.0001$) in cows treated with GONAbreed (33.4%) than the pregnancy rate to FTAI in cows treated with water (13.6%), following the synchronization protocol with cloprostenol sodium.

BEEF COWS: The effectiveness of GONAbreed (gonadorelin acetate) for use with injectable 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 GONAbreed (1 mL; 100 µg gonadorelin as the acetate salt) and 342 cows were administered an equivalent volume of water as an intramuscular injection twice in the following regimen:

Day 0: 1 mL GONAbreed or sterile water for injection
Day 7: 500 µg cloprostenol (as cloprostenol sodium)
Day 9/10: 1 mL GONAbreed or sterile water for injection

Day 9/10 injections took place approximately 60 hours after the Day 7 cloprostenol injection.
Fixed time AI was performed immediately after the Day 9/10 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 GONAbreed (21.7%) than the pregnancy rate to FTAI in cows treated with water (7.4%) when used in a synchronization protocol with cloprostenol sodium.

Storage: Store unopened vials refrigerated at 2-8˚C. Once broached, product may be stored at temperatures up to 25˚C. Discard remaining product 180 days after first use. Keep from freezing.

Presentation: GONAbreed is supplied in multi-dose glass vials containing 20 mL and 100 mL of sterile solution.

Product Code:
900091 (20 mL), 900092 (100 mL)