PARNELL®

living SCIENCE

Highest concentration of GnRH on the market

Increase efficiency with GONAbreed®

- More active ingredient in a 1 mL dose than some competitors have in a 2 mL dose
- More doses per bottle for efficiency and quicker administration
- Designed for compliance
- Consistent product and supply

Be CONFIDENT you will get great results for your farms fertility program

- Supplying fertility treatments to over 15 countries for over 20 years
- More than 60 million doses sold worldwide

To learn more about GONAbreed or other Parnell offerings, contact your Parnell representative.

GONAbreed®
(gonadorelin acetate)

100 mcg/mL gonadorelin acetate Injectable Solution

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 cows and beef cows.

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

DESCRIPTION:

GONAbreed is a sterile solution containing 100 micrograms of 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 –

a molecular weight of 1182.32 and empirical formula $C_{55}H_{75}N_{17}O_{13}$. The acetate salt has a molecular weight of 60.05 and an empirical formula $C_{55}H_{75}N_{17}O_{13}.C_2H_4O_2$.

Each mL of GONAbreed contains:
Gonadorelin (as gonadorelin acetate) 100 mcg
Benzyl alcohol 10 mg
Sodium chloride 7.47 mg
Sodium phosphate monobasic 8.3 mg
Sodium phosphate dibasic 4.8 mg
Water for injection, q.s.
pH adjusted with hydrochloric acid or sodium hydroxide.

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

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

Reproductive Synchrony

GONAbreed 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 GONAbreed is 100 mcg gonadorelin acetate (1 mL) per cow.

Reproductive Synchrony

The intramuscular dosage of GONAbreed is 100 mcg gonadorelin acetate (1 mL) per cow, used in reproductive synchrony programs similar to the following:

1. Administer the first GONAbreed injection (1 mL) at Time 0.
2. Administer 500 mcg cloprostenol (as cloprostenol sodium) by intramuscular injection 6 to 8 days after the first GONAbreed injection.
3. Administer the second GONAbreed injection (1 mL) 30 to 72 hours after the cloprostenol sodium injection.
4. Perform FTAI 0 to 24 hours after the second GONAbreed injection or inseminate cows on detected estrus using standard herd practices.
5. **WARNINGS AND PRECAUTIONS:**
6. **Not for use in humans.**
7. **Keep out of reach of children.**
8. **WITHDRAWAL PERIODS:**
9. **No withdrawal period or milk discard time is required when used according to the labeling.**
10. To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Parnell at 1-800-88-PARNELL (1-800-887-2763). For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae
11. **PHARMACOLOGY AND TOXICOLOGY:**
12. Endogenous gonadorelin is synthesized 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 affect the release of gonadotrophins (e.g. LH, FSH). Synthetic gonadorelin administered intravenously or intramuscularly also causes the release of endogenous LH or FSH from the anterior pituitary.
13. 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 adverse effects were noted among rats or dogs administered 120 mcg/kg/day or 72 mcg/kg/day intravenously for 15 days.
14. 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.
15. The intravenous administration of 60 mcg/kg/day of gonadorelin acetate to pregnant rats and rabbits during organogenesis did not cause embryotoxic or teratogenic effects.
16. Further, gonadorelin 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 gonadorelin was established through review and evaluation of extensive published literature available for the use of gonadorelin-containing products.

The intramuscular administration of 1000 mcg gonadorelin 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 gonadorelin for the treatment of ovarian follicular cysts, the incidence of health abnormalities was not significantly greater in cows administered gonadorelin than cows administered a placebo injection.

The target animal safety of, and injection site reactions to, GONAbreed 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 GONAbreed than cows administered a placebo injection.

EFFECTIVENESS:

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

The effectiveness of GONAbreed (gonadorelin acetate) 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 GONAbreed (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: 1 mL GONAbreed or sterile water for injection Day 7: 500 mcg cloprostenol (as cloprostenol sodium) Day 9: 1 mL GONAbreed 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 GONAbreed (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 GONAbreed (gonadorelin acetate) 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 GONAbreed (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: 1 mL GONAbreed or sterile water for injection Day 7: 500 mcg cloprostenol (as cloprostenol sodium) Day 9: 1 mL GONAbreed 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 GONAbreed (21.7%) than the pregnancy rate to FTAI in cows treated with water (7.4%).

HOW SUPPLIED:

GONAbreed is available in a concentration of 100 mcg/mL gonadorelin acetate.
GONAbreed is supplied in multidose vials containing 20 mL and 100 mL of sterile solution.

STORAGE, HANDLING, AND DISPOSAL:

Discard remaining product 180 days after first use. Once broached, product may be stored at temperatures up to 25°C (77°F).
KEEP UNOPENED VIALS REFRIGERATED: 2° - 8°C (36° - 46°F).

Manufactured by:
PARNELL TECHNOLOGIES PTY. LTD.
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Alexandria NSW 2015
Australia
Owner of the registered trademark GONAbreed®

Distributed by:
PARNELL U.S. 1, Inc.
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Overland Park, KS, 66211

Approved by FDA under ANADA # 200-541

20mL & 100mL:
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