Date of Approval: July 5, 2019

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 113-645

Estrumate®

Cloprostenol injection

Injectable solution

Lactating dairy cows

This supplement provides for addition of the indication
'For use with Fertagyl® (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.'

Sponsored by:

Intervet, Inc.

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I. GENERAL INFORMATION

A. File Number

NADA 113-645

B. Sponsor

Intervet, Inc.,
2 Giralda Farms,
Madison, NJ 07940

Drug Labeler Code: 000061

C. Proprietary Name

Estrumate®

D. Drug Product Established Name

Cloprostenol injection

E. Pharmacological Category

Prostaglandin

F. Dosage Form

Injectable solution

G. Amount of Active Ingredient

250 mcg cloprostenol/mL (equivalent to 263 mcg cloprostenol sodium/mL)

H. How Supplied

20 mL and 100 mL multidose vials

I. Dispensing Status

Rx

J. Dosage Regimen

For use with Fertagyl® (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.

Use in reproductive synchrony programs similar to the following:

- Administer the first Fertagyl® injection (2 mL; 86 mcg gonadorelin, as gonadorelin acetate) by intramuscular injection on Day 0.
- Administer 2 mL of Estrumate by intramuscular injection 6 to 8 days after the first Fertagyl® injection.
- Administer the second Fertagyl® injection (2 mL; 86 mcg gonadorelin, as gonadorelin acetate) 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.

K. Route of Administration

Intramuscular

L. Species/Class

Lactating dairy cows

M. Indication

For use with Fertagyl® (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.

N. Effect of Supplement

This supplement provides for addition of the indication 'For use with Fertagyl® (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.'

II. EFFECTIVENESS

A. Dosage Characterization

This supplemental approval does not change the previously approved dosage. NADA 113-645 contains summaries of studies that characterize the dosage of Estrumate® in lactating dairy cows (48 FR 15619, dated April 12, 1983). The Freedom of Information (FOI) Summary for the supplemental approval of ANADA 200-134 (under section 512(b)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)) dated April 23, 2015, contains dosage characterization information for the use of Fertagyl® (gonadorelin) with Estrumate® (cloprostenol injection) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.

B. Substantial Evidence

NADA 113-645 contains summaries of studies that demonstrate effectiveness of Estrumate® for lactating dairy cows (48 FR 15619, dated April 12, 1983). The FOI Summary for the supplemental approval of ANADA 200-134 (under section 512(b)(1) of the FD&C Act) dated April 23, 2015, contains a summary of studies that demonstrate effectiveness of Fertagyl® (gonadorelin) for use with Estrumate® (cloprostenol injection) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.

III. TARGET ANIMAL SAFETY

NADA 113-645 contains summaries of target animal safety studies for Estrumate® for lactating dairy cows (48 FR 15619, dated April 12, 1983). The FOI Summary for the supplemental approval of ANADA 200-134 (under section 512(b)(1) of the FD&C Act) dated April 23, 2015, contains a summary of target animal safety information for Fertagyl® (gonadorelin) with Estrumate® (cloprostenol injection) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.

IV. HUMAN FOOD SAFETY

A. Antimicrobial Resistance

The Agency evaluated the need to address the impact of the use of cloprostenol and gonadorelin on microbial food safety (antimicrobial resistance) among bacteria of public health concern in or on cloprostenol and gonadorelin-treated cattle. We considered that:

1) Cloprostenol and gonadorelin are not regularly considered to have properties that would exert antimicrobial resistance pressure towards the emergence or selection of bacteria of public health concern;

2) Cloprostenol and gonadorelin are not used to treat gastroenteritis or other bacterial diseases in humans;

3) Cloprostenol and gonadorelin (or similar compounds) are not under development to treat bacterial diseases in humans; and

4) Cloprostenol and gonadorelin are not indicated for a bacterial disease in a food-producing animal species.

Therefore, the Agency determined there was no need to develop or submit for review additional microbial food safety (antimicrobial resistance) information regarding this proposed use of cloprostenol and gonadorelin in cattle.

B. Toxicology

A toxicological acceptable daily intake (ADI), a final ADI and safe concentrations for total residues of cloprostenol and gonadorelin were not needed for this supplemental approval. NADA 113-645 contains summaries of all toxicology studies and information supporting the original and supplemental approvals of cloprostenol sodium in cattle (47 FR 4678, dated February 2, 1982, and 48 FR 15619, dated April 12, 1983). The FOI Summary for the original approval of ANADA 200-134, dated June 17, 1996, contains safety information for gonadorelin acetate. Reassessment of the toxicology and safety information was not needed for this supplemental approval.

C. Residue Chemistry

NADA 113-645 contains summaries of residue chemistry studies supporting the original and supplemental approvals of cloprostenol sodium in cattle (47 FR 4678, dated February 2, 1982, and 48 FR 15619, dated April 12, 1983). The FOI Summary for the original approval of ANADA 200-134, dated June 17, 1996, contains a summary of residue chemistry studies and information for gonadorelin acetate in cattle. The FOI Summary for the supplemental approval of ANADA 200-134 (under section 512(b)(1) of the FD&C Act), dated April 23, 2015, contains a summary of residue chemistry studies and information for cloprostenol sodium and gonadorelin acetate in cattle.

D. Analytical Method for Residues

Because there are no tolerances required for either cloprostenol or gonadorelin, no regulatory methods are required.

V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Estrumate®:

Not for use in humans. Keep this and all drugs out of the reach of children. Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. Estrumate is readily absorbed through the skin and can cause abortion and/or bronchospasms. Direct contact with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

To obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, contact Merck Animal Health at 1-800-211-3573 or http://www.merck.com

The product labeling for Fertagyl® contains the following information regarding safety to humans handling, administering, or exposed to Fertagyl®:

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

VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the FD&C Act and 21 CFR part 514. The data demonstrate that Estrumate®, when used according to the label, is safe and effective for use with Fertagyl® (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows. Additionally, data demonstrate that residues in food products derived from species treated with Estrumate® will not represent a public health concern when the product is used according to the label.

A. Marketing Status

This product may be dispensed only by or on the lawful order of a licensed veterinarian (Rx marketing status). Adequate directions for lay use cannot be written because veterinary experience is required to safely administer the product, and because the use of this product for the synchronization of estrous cycles requires the use of Fertagyl®, which also has Rx marketing status.

B. Exclusivity

This supplemental approval for Estrumate® qualifies for THREE years of marketing exclusivity under section 512(c)(2)(F)(iii) of the FD&C Act because the supplemental application included effectiveness studies for the use of Estrumate® (cloprostenol injection) with Fertagyl® to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows, which were originally reported in the FOI Summary for the supplemental approval of ANADA 200-134 (under section 512(b)(1) of the FD&C Act) dated April 23, 2015. This exclusivity begins as of the date of our approval letter and only applies to the indication for use with Fertagyl® (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.

C. Supplemental Applications

This supplemental NADA required a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(2)).

D. Patent Information

For current information on patents, see the Animal Drugs @ FDA database or the Green Book on the FDA CVM internet website.