

C HEA-305

MAY 13 2004

Date of Approval:

## **FREEDOM OF INFORMATION SUMMARY**

### **ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION (ANADA)**

**ANADA 200-310**

**ESTROPLAN Injection**

(cloprostenol sodium)

Beef and Dairy Cattle

It is indicated for intramuscular use to induce luteolysis in beef and dairy cattle. The luteolytic action of ESTROPLAN can be utilized to manipulate the estrous cycle to better fit certain management practices, to terminate pregnancies resulting from mismatings, and to treat certain conditions associated with prolonged luteal function.

Sponsored by:  
Parnell Laboratories (Aust) Pty. Ltd.  
Century Estate, Unit 6  
476 Gardeners Road  
Alexandria, New South Wales 2015, Australia

200-310

FOIS 1

FREEDOM OF INFORMATION SUMMARY

**1. General Information:**

- a. File Number: ANADA 200-310
- b. Sponsor: Parnell Laboratories (Aust) Pty. Ltd.  
Century Estate, unit 6  
476 Gardeners Road  
Alexandria, New South Wales 2015, Australia  
  
Drug Labeler Code: 068504
- c. Established Name: Cloprostenol sodium
- d. Proprietary Name: ESTROPLAN Injection
- e. Dosage Form: Injectable
- f. How Supplied: 20 mL multidose vials
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: Each mL of the colorless aqueous solution contains 263 mcg of cloprostenol sodium equivalent to 250 mcg of cloprostenol.
- i. Route of Administration: Intramuscularly
- j. Species/Class: Beef cattle & dairy cattle
- k. Recommended Dosage: 2 mL of ESTROPLAN Injection (500 mcg cloprostenol) should be administered by intramuscular injection for all indications in both beef and dairy cattle.
- l. Pharmacological Category: Luteolytic action
- m. Indications: It is indicated for intramuscular use to induce luteolysis in beef and dairy cattle. The luteolytic action of ESTROPLAN can be utilized to manipulate the estrous cycle to better fit certain management



**4. AGENCY CONCLUSIONS:**

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the Act and demonstrates that ESTROPLAN Injection, when used under its proposed conditions of use, is safe and effective for its labeled indications.

**5. ATTACHMENTS:**

Facsimile Generic Labeling and Currently Approved Pioneer Labeling are attached as indicated below:

Pioneer Labeling for NADA 113-645:  
ESTRUMATE- 20 mL insert and box

Generic Labeling for ANADA 200-310  
ESTROPLAN Injection-20 mL insert, box, and shipping carton



TOP, BACK AND SIDE  
PANELS

3 0 9



Schering-Plough Animal Health

PROTECT FROM LIGHT. STORE IN CARTON. STORE AT CONTROLLED ROOM TEMPERATURE 59°-86°F (15°-30°C).

Equivalent to 250 mcg cloprostenol / mL

# Estrumate<sup>®</sup> (cloprostenol sodium)

10 x 20 mL Vials

10 x 20 mL Vials

## Estrumate<sup>®</sup> (cloprostenol sodium)

An Analogue of Prostaglandin F<sub>2α</sub>  
for Intramuscular Injection in Beef and Dairy Cattle

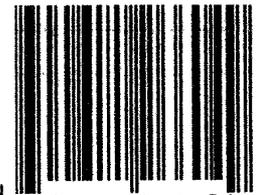
Equivalent to 250 mcg cloprostenol / mL

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

 Schering-Plough Animal Health

Copyright © 1999, Schering-Plough Animal Health Corp., Union, NJ 07083. All rights reserved. 23507226 Rev. 3/00

Each mL of the colorless aqueous solution contains 263 mcg of cloprostenol sodium (equivalent to 250 mcg. of cloprostenol) in a sodium citrate, anhydrous citric acid, and sodium chloride buffer containing 0.1% w/v chlorocresol BP as a bactericide. pH is adjusted, as necessary, with sodium hydroxide or citric acid.  
Read insert before using this drug.  
**FOR VETERINARY USE ONLY**



N 3 0061-1266-04 9

10 x 20 mL Vials

# Estrumate® (cloprostenol sodium)

An Analogue of Prostaglandin F<sub>2α</sub>  
for Intramuscular Injection in Beef and Dairy Cattle

Equivalent to 250 mcg cloprostenol/mL

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



Schering-Plough Animal Health

**INDICATIONS:** For intramuscular use to induce luteolysis in beef and dairy cattle. The luteolytic action of Estrumate can be utilized to manipulate the estrous cycle to better fit certain management practices, to terminate pregnancies resulting from mismatings, and to treat certain conditions associated with prolonged luteal function.

**DOSAGE AND ADMINISTRATION:** 2 mL of Estrumate (500 mcg of cloprostenol) should be administered by INTRAMUSCULAR INJECTION for all indications.

**WARNING:** Women of child-bearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. In the early stages, women may be unaware of their pregnancies. Estrumate is readily absorbed through the skin and may 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.

FRONT AND SIDE  
PANELS

Estrumate®  
(cloprostenol sodium)

Estrumate®  
(cloprostenol sodium)

An Analogue of Prostaglandin  
F<sub>2α</sub> for Intramuscular Injection  
in Beef and Dairy Cattle

Equivalent to 250 mcg cloprostenol/mL

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

FOR VETERINARY USE ONLY

20 mL 10 Doses

Schering-Plough  
Animal Health

**WARNING:** For veterinary use only. Women of child-bearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. In the early stages, women may be unaware of their pregnancies. Estrumate is readily absorbed through the skin and may 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.

NDG 0061-1266-02

20 mL

Estrumate®  
(cloprostenol sodium)

An Analogue of  
Prostaglandin F<sub>2α</sub> for  
Intramuscular Injection  
in Beef and Dairy Cattle.

Equivalent to 250 mcg  
cloprostenol/mL

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

FOR VETERINARY USE ONLY

20 mL 10 Doses

Schering-Plough  
Animal Health

**INDICATIONS:** For intramuscular use to induce luteolysis in beef and dairy cattle. The luteolytic action of Estrumate can be utilized to manipulate the estrous cycle to better fit certain management practices, to terminate pregnancies resulting from mismatings, and to treat certain conditions associated with prolonged luteal function.

**DOSAGE AND ADMINISTRATION:** 2 mL of Estrumate (500 mcg of cloprostenol) should be administered by INTRAMUSCULAR INJECTION for all indications.

READ INSERT BEFORE USING THIS DRUG. PROTECT FROM LIGHT. STORE IN THIS CONTAINER. STORE AT CONTROLLED ROOM TEMPERATURE 59°-86°F (15°-30°C).

Each mL of the colorless aqueous solution contains 253 mcg of cloprostenol sodium (equivalent to 250 mcg of cloprostenol) in a sodium citrate, anhydrous citric acid, and sodium chloride buffer containing 0.1% w/v chlorocresol BP as a bactericide. pH is adjusted, as necessary, with sodium hydroxide or citric acid.

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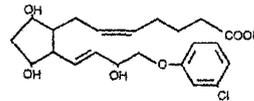
# Estrumate®

(cloprostenol sodium)

## Prostaglandin Analogue for Cattle

Equivalent to 250 mcg cloprostenol/mL

Estrumate® (cloprostenol sodium) is a synthetic prostaglandin analogue structurally related to prostaglandin F<sub>2</sub> α (PGF<sub>2</sub> α). Each mL of the colorless aqueous solution contains 263 mcg of cloprostenol sodium (equivalent to 250 mcg of cloprostenol) in a sodium citrate, anhydrous citric acid and sodium chloride buffer containing 0.1% w/v chlorocresol BP as a bactericide. pH is adjusted, as necessary, with sodium hydroxide or citric acid.



### ACTION:

Estrumate causes functional and morphological regression of the corpus luteum (luteolysis) in cattle. In normal, nonpregnant cycling animals, this effect on the life span of the corpus luteum usually results in estrus 2 to 5 days after treatment. In animals with prolonged luteal function (pyometra, mummified fetus, and luteal cysts), the induced luteolysis usually results in resolution of the condition and return to cyclicity. Pregnant animals may abort depending on the stage of gestation.

### INDICATIONS:

For intramuscular use to induce luteolysis in beef and dairy cattle. The luteolytic action of Estrumate can be utilized to manipulate the estrous cycle to better fit certain management practices, to terminate pregnancies resulting from mismatings, and to treat certain conditions associated with prolonged luteal function.

### RECOMMENDED USES:

#### Unobserved or nondetected estrus

Cows which are not detected in estrus, although ovarian cyclicity continues, can be treated with Estrumate if a mature corpus luteum is present. Estrus is expected to occur 2 to 5 days following injection, at which time animals may be inseminated. Treated cattle should be inseminated at the usual time following detection of estrus. If estrus detection is not desirable or possible, treated animals may be inseminated twice at about 72 and 96 hours postinjection.

#### Pyometra or Chronic Endometritis

Damage to the reproductive tract at calving or postpartum retention of the placenta often leads to infection and inflammation of the uterus (endometritis). Under certain circumstances, this may progress into chronic endometritis with the uterus becoming distended with purulent matter. This condition, commonly referred to as pyometra, is characterized by a lack of cyclical estrous behavior and the presence of a persistent corpus luteum. Induction of luteolysis with Estrumate usually results in evacuation of the uterus and a return to normal cyclical activity within 14 days after treatment. After 14 days posttreatment, recovery rate of treated animals will not be different than that of untreated cattle.

#### Mummified Fetus

Death of the conceptus during gestation may be followed by its degeneration and dehydration. Induction of luteolysis with Estrumate usually results in expulsion of the mummified fetus from the uterus. (Manual assistance may be necessary to remove the fetus from the vagina.) Normal cyclical activity usually follows.

#### Luteal Cysts

A cow may be noncyclic due to the presence of a luteal cyst (a single, anovulatory follicle with a thickened wall which is accompanied by no external signs and by no changes in palpable consistency of the uterus). Treatment with Estrumate can restore normal ovarian activity by causing regression of the luteal cyst.

#### Pregnancies from Mismating

Unwanted pregnancies can be safely and efficiently terminated from 1 week after mating until about 5 months of gestation. The induced abortion is normally uncomplicated and the fetus and placenta are usually expelled about four to five days after the injection with the reproductive tract returning to normal soon after the abortion. The ability of Estrumate to induce abortion decreases beyond the fifth month of gestation while the risk of dystocia and its consequences increases. Estrumate has not been sufficiently tested under feedlot conditions; therefore, recommendations cannot be made for its use in heifers placed in feedlots.

#### Controlled Breeding

The luteolytic action of Estrumate can be utilized to schedule estrus and ovulation for an individual cycling animal or a group of animals. This allows control of the time at which cycling cows or heifers can be bred. Estrumate can be incorporated into a controlled breeding program by the following methods:

1. Single Estrumate injection; only animals with a mature corpus luteum should be treated to obtain maximum response to the single injection. However, not all cycling cattle should be treated since a mature corpus luteum is present for only 11 to 12 days of the 21-day cycle.

Prior to treatment, cattle should be examined rectally and found to be anatomically normal, be nonpregnant, and have a mature corpus luteum. If these criteria are met, estrus is expected to occur 2 to 5 days following injection, at which time animals may be inseminated. Treated cattle should be inseminated at the usual time following

detection of estrus. If estrous detection is not desirable or possible, treated animals may be inseminated either once at about 72 hours or twice at about 72 and 96 hours postinjection.

With a single injection program, it may be desirable to assess the cyclicity status of the herd before Estrumate treatment. This can be accomplished by heat detecting and breeding at the usual time following detection of estrus for a 6-day period, all prior to injection. If by the sixth day the cyclicity status appears normal (approximately 25%-30% detected in estrus), all cattle not already inseminated should be palpated for normality, nonpregnancy, and cyclicity, then injected with Estrumate. Breeding should then be continued at the usual time following signs of estrus on the seventh and eighth day. On the ninth and tenth day, breeding may continue at the usual time following detection of estrus or all cattle not already inseminated may be bred either once on the ninth day (at about 72 hours postinjection) or on both the ninth and tenth day (at about 72 and 96 hours postinjection).

2. Double Estrumate injections: prior to treatment, cattle should be examined rectally and found to be anatomically normal, nonpregnant, and cycling (the presence of a mature corpus luteum is not necessary when the first injection of a double injection regimen is given). A second injection should be given 11 days after the first injection. In normal, cycling cattle, estrus is expected 2 to 5 days following the second injection. Treated cattle should be inseminated at the usual time following detection of estrus. If estrous detection is not desirable or possible, treated animals may be inseminated either once at about 72 hours or twice at about 72 and 96 hours following the second Estrumate injection.

Many animals will come into estrus following the first injection; these animals can be inseminated at the usual time following detected estrus. Animals not inseminated should receive a second injection 11 days after the first injection. Animals receiving both injections may be inseminated at the usual time following detection of estrus or may be inseminated either once at about 72 hours or twice at about 72 and 96 hours post second injection.

- Any controlled breeding program recommended should be completed by either:
- observing animals (especially during the third week after injection) and inseminating or hand mating any animals returning to estrus,
  - OR
  - turning in clean-up bull(s) 5 to 7 days after the last injection of Estrumate to cover any animals returning to estrus.

#### REQUIREMENTS FOR CONTROLLED BREEDING PROGRAMS:

A variety of programs can be designed to best meet the needs of individual management systems. A controlled breeding program should be selected which is appropriate for the existing circumstances and management practices.

Before a controlled breeding program is planned the producer's objectives must be examined and he must be made aware of the projected results and limitations. The producer and his consulting veterinarian should review the operation's breeding history, herd health and nutritional status, and agree that a controlled breeding program is practical in the producer's specific situation. For any successful controlled breeding program:

- cows and heifers must be normal, nonpregnant, and cycling (rectal palpation should be performed)
- cattle must be in a fit and thrifty breeding condition and on an adequate or increasing plane of nutrition.
- proper program planning and record keeping are essential
- if artificial insemination is used it must be performed by competent inseminators using high-quality semen.

It is important to understand that Estrumate is effective only in animals with a mature corpus luteum (ovulation must have occurred at least 5 days prior to treatment). This must be considered when breeding is intended following a single Estrumate injection.

#### SAFETY AND TOXICITY:

At 50 and 100 times the recommended dose, mild side effects may be detected in some cattle. These include increased uneasiness, slight frothing, and milk let-down.

#### CONTRAINDICATIONS:

Estrumate should not be administered to a pregnant animal whose calf is not to be aborted.

#### PRECAUTIONS:

There is no effect on fertility following the single or double dosage regimen when breeding occurs at induced estrus or at 72 and 96 hours posttreatment. Conception rates may be lower than expected in those fixed time breeding programs which omit the second insemination (i.e., the insemination at or near 96 hours). This is especially true if a fixed time insemination is used following a single Estrumate injection. As with all parenteral products, careful aseptic techniques should be employed to decrease the possibility of postinjection bacterial infection. Antibiotic therapy should be employed at the first sign of infection.

#### DOSAGE AND ADMINISTRATION:

2 mL of Estrumate (500 mcg of cloprostenol) should be administered by *INTRAMUSCULAR INJECTION* for all indications in both beef and dairy cattle.

#### WARNINGS:

For veterinary use only.

Women of child-bearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. In the early stages, women may be unaware of their pregnancies. Estrumate is readily absorbed through the skin and may 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.

#### STORAGE CONDITIONS:

1. Protect from light.
2. Store in container.
3. Store at controlled room temperature 59°-86°F. (15°-30°C.).

#### HOW SUPPLIED:

20-mL multidose vials

#### CAUTION:

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

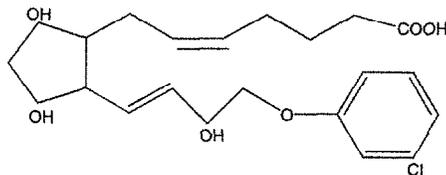
## estroPLAN™ injection

(cloprostenol sodium)

Prostaglandin Analogue for Cattle

Equivalent to 250 mcg cloprostenol/mL

estroPLAN injection (cloprostenol sodium) is a synthetic prostaglandin analogue structurally related to prostaglandin F<sub>2α</sub> (PGF<sub>2α</sub>). Each mL of the colorless aqueous solution contains 263 mcg of cloprostenol sodium (equivalent to 250 mcg of cloprostenol), chlorocresol 1.0 mg as a bactericide, citric acid anhydrous 0.66 mg, sodium citrate 5.03 mg, sodium chloride 6.76 mg. The pH is adjusted, as necessary, with sodium hydroxide or citric acid.



### ACTION:

estroPLAN injection causes functional and morphological regression of the corpus luteum (luteolysis) in cattle. In normal, nonpregnant cycling animals this effect on the life span of the corpus luteum usually results in estrus 2 to 5 days after treatment. In animals with prolonged luteal function (pyometra, mummified fetus, and luteal cysts) the induced luteolysis usually results in resolution of the condition and return to cyclicity. Pregnant animals may abort depending on the stage of gestation.

### INDICATIONS:

For intramuscular use to induce luteolysis in beef and dairy cattle. The luteolytic action of estroPLAN injection can be utilized to manipulate the estrus cycle to better fit certain management practices, to terminate pregnancies resulting from mismatings and to treat certain conditions associated with prolonged luteal function.

### RECOMMENDED USES:

#### Unobserved or Non-detected Estrus

Cows which are not detected in estrus, although ovarian cyclicity continues, can be treated with estroPLAN if a mature corpus luteum is present. Estrus is expected to occur 2 to 5 days following injection, at which time animals may be inseminated. Treated cattle should be inseminated at the usual time following detection of estrus. If estrus detection is not desirable or possible, treated animals may be inseminated twice at about 72 and 96 hours post injection.

#### Pyometra or Chronic Endometritis

Damage to the reproductive tract at calving or post partum retention of the placenta often leads to infection and inflammation of the uterus (endometritis). Under certain circumstances, this may progress into chronic endometritis with the uterus becoming distended with purulent matter. This condition, commonly referred to as pyometra, is characterized by a lack of cyclical estrus behavior and the presence of a persistent corpus luteum. Induction of luteolysis with estroPLAN usually results in evacuation of the uterus and a return to normal cyclical activity within 14 days after treatment. After 14 days post treatment, recovery rate of treated animals will not be different than that of untreated cattle.

#### Mummified Fetus

Death of the conceptus during gestation may be followed by its degeneration and dehydration. Induction of luteolysis with estroPLAN usually results in expulsion of the mummified fetus from the uterus. (Manual assistance may be necessary to remove the fetus from the vagina.) Normal cyclical activity usually follows.

#### Luteal Cysts

A cow may be noncyclic due to the presence of a luteal cyst (a single, anovulatory follicle with a thickened wall which is accompanied by no external signs and by no changes in palpable consistency of the uterus). Treatment with estroPLAN can restore normal ovarian activity by causing regression of the luteal cyst.

#### Pregnancies from Mismatching

Unwanted pregnancies can be safely and efficiently terminated from 1 week after mating until about five months of gestation. The induced abortion is normally uncomplicated and the fetus and placenta are usually expelled about four to five days after the injection with the reproductive tract returning to normal soon after the abortion. The ability of estroPLAN to induce abortion decreases beyond the fifth month of gestation while the risk of dystocia and its consequences increases. estroPLAN has not been sufficiently tested under feedlot conditions, therefore recommendations cannot be made for its use in heifers placed in feedlots.

#### Controlled Breeding

The luteolytic action of estroPLAN can be utilized to schedule estrus and ovulation for an individual cycling animal or a group of animals. This allows control of the time at which cycling cows or heifers can be bred.

estroPLAN can be incorporated into a controlled breeding program by the following methods:

##### 1. Single estroPLAN Injection

Only animals with a mature corpus luteum should be treated to obtain maximum response to the single injection. However, not all cycling cattle should be treated since a mature corpus luteum is present for only 11 to 12 days of the 21-day cycle.

Prior to treatment, cattle should be examined rectally and found to be anatomically normal, be non-pregnant and have a mature corpus luteum. If these criteria are met, estrus is expected to occur two to five days following injection, at which time animals may be inseminated. Treated cattle should be inseminated at the usual time following detection of estrus. If estrus detection is not desirable or possible, treated animals may be inseminated either once at about 72 hours or twice at about 72 and 96 hours post injection.

With a single injection program, it may be desirable to assess the cyclicity status of the herd before estroPLAN treatment. This can be accomplished by heat detecting and breeding at the usual time following detection of estrus for a 6-day period, all prior to injection. If by the sixth day the cyclicity status appears normal (approximately 25–30% detected in estrus), all cattle not already inseminated should be palpated for normality, non-pregnancy, and cyclicity, then injected with estroPLAN. Breeding should then be continued at the usual time following signs of estrus on the seventh and eighth day. On the ninth and tenth day breeding may continue at the usual time following detection of estrus or all cattle not already inseminated may be bred either once on the ninth day (at about 72 hours post injection) or on both the ninth and tenth day (at about 72 and 96 hours post injection).

460153  
818 482 000

NDC 0009-5212-01  
**estroPLAN™** Injection  
 (cloprostenol sodium)  
 Equivalent to 250 mcg cloprostenol/mL  
 CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian  
 10 Doses 20mL  
 ANADA 200-310, Approved by FDA  
 Distributed by  
 Pfizer Inc  
 235E 42nd Street, New York, NY 10017

An analogue of prostaglandin F<sub>2α</sub> for Intramuscular Injection in beef and dairy cattle.  
 Read insert before using this drug  
 STORE AT CONTROLLED ROOM TEMPERATURE 20° - 25°C (68° - 77°F)  
 PROTECT FROM LIGHT. STORE IN CARTON  
 FOR VETERINARY USE ONLY  
 Each mL of the colorless aqueous solution contains 263 mcg of cloprostenol sodium (equivalent to 250 mcg of cloprostenol), chloroCresol 1.0 mg as a bactericide, citric acid anhydrous 0.66 mg, sodium citrate 5.03 mg, sodium chloride 6.76 mg. The pH is adjusted, as necessary, with sodium hydroxide or citric acid

**Parnell**

460152  
 816 460 000

**Wayne Pharma  
 Design Specifications**

customer: Parnell  
 container: 1 x 20 mL glass vial  
 product code: 9610A-US

template: 880709/1  
 dimensions: 95 x 30 mm  
 barcode magnification: 1x/0

application: illustrator  
 saved version: 8.0  
 platform: windows

colours:  320 C (green)  
 Black C  
 UV

Have you checked the artwork in accordance to your OI template? Once you have signed the artwork you will be responsible for it proceeding to the printing stage.  
 M marketing RA regulatory affairs P production IP intellectual property L legal MI medical information FP final proofing Q quality

designer  
 \_\_\_\_\_ 19/09/02 ed.  
 \_\_\_\_\_ 29/10/02 ed.  
 \_\_\_\_\_ 30/10/03 ed.

M: \_\_\_\_\_ / / RA: \_\_\_\_\_ / /  
 P: \_\_\_\_\_ / / IP: \_\_\_\_\_ / /



Equivalent to 250 mcg cloprostenol/mL  
 (cloprostenol sodium)  
**estroPLAN™**  
 Injection  
 NDC 0009-5212-01

**INDICATIONS:**  
 For intramuscular use to induce luteolysis in beef and dairy cattle. The luteolytic action of **estroPLAN** injection can be utilized to manipulate the estrus cycle to better fit certain management practices, to terminate pregnancies resulting from mismatings and to treat certain conditions associated with prolonged luteal function.

**DOSAGE AND ADMINISTRATION:**  
 2 mL of **estroPLAN** injection (500 mcg of cloprostenol) should be administered by INTRAMUSCULAR INJECTION for all indications. READ INSERT BEFORE USING THIS DRUG. PROTECT FROM LIGHT. STORE IN THIS CONTAINER. STORE AT CONTROLLED ROOM TEMPERATURE 20° - 25°C (68° - 77°F).

Each mL of the colorless aqueous solution contains 263 mcg of cloprostenol sodium (equivalent to 250 mcg of cloprostenol), chlorocresol 1.0 mg as a bactericide, citric acid anhydrous 0.66 mg, sodium citrate 5.05 mg, sodium chloride 6.76 mg. The pH is adjusted, as necessary, with sodium hydroxide or citric acid.

**WARNING:**  
 For veterinary use only. Women of child-bearing age, asthmatics and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. In the early stages women may be unaware of their pregnancies. **estroPLAN** is readily absorbed through the skin and may 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.

NDC 0009-5212-01

**estroPLAN™**  
 Injection  
 (cloprostenol sodium)



An analogue of prostaglandin F<sub>2α</sub> for intramuscular injection in beef and dairy cattle.

Equivalent to 250 mcg cloprostenol/mL

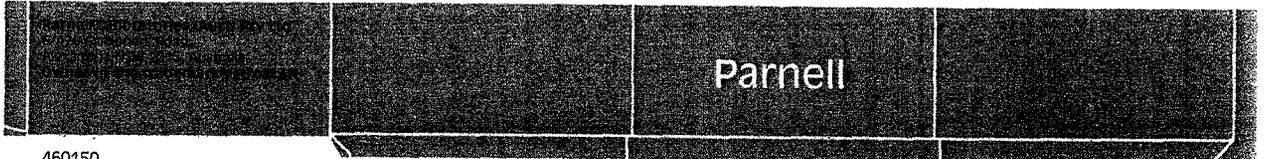
**CAUTION:** Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

FOR VETERINARY USE ONLY

20mL 10 doses

ANADA 200-310 Approved by FDA.

Distributed by  
**Pfizer Inc**  
 235 E 42nd Street  
 New York, NY, 10017



460150  
 818 481 000



**Mayne Pharma  
 Design Specifications**

customer: Parnell  
 container: 1 x 20 mL glass vial  
 product code: 9610A-US

template: 880532/1  
 dimensions: 39.5 x 39.5 x 80.5  
 barcode magnification: 100%

application: illustrator  
 saved version: 8.0  
 platform: windows

colours: 320 C (green)  
 Black C  
 All text and graphics will be UV Varnished

Have you checked the artwork in accordance to your OI template? Once you have signed the artwork you will be responsible for it proceeding to the printing stage.  
 M marketing RA regulatory affairs P production IP intellectual property L legal MI medical information FP final proofing Q quality

M: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ RA: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
 P: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_

designer  
 \_\_\_\_\_ 19/09/02 ed.  
 \_\_\_\_\_ 28/10/02 ed.

## estroPLAN™ injection

### 2. Double estroPLAN injections

Prior to treatment, cattle should be examined rectally and found to be anatomically normal, non-pregnant, and cycling (the presence of a mature corpus luteum is not necessary when the first injection of a double injection regimen is given). A second injection should be given 11 days after the first injection. In normal, cycling cattle, estrus is expected 2 to 5 days following the second injection. Treated cattle should be inseminated at the usual time following detection of estrus if estrus detection is not desirable or possible, treated animals may be inseminated either once at about 72 hours or twice at about 72 and 96 hours following the second estroPLAN injection.

Many animals will come into estrus following the first injection, these animals can be inseminated at the usual time following detected estrus. Animals not inseminated should receive a second injection 11 days after the first injection. Animals receiving both injections may be inseminated at the usual time following detection of estrus or may be inseminated either once at about 72 hours or twice at about 72 and 96 hours post second injection.

Any controlled breeding program recommended should be completed by either

- observing animals (especially during the third week after injection) and inseminating or hand mating any animals returning to estrus, or
- turning in clean-up bull(s) 5 to 7 days after the last injection of estroPLAN to cover any animals returning to estrus.

### REQUIREMENTS FOR CONTROLLED BREEDING PROGRAMS:

A variety of programs can be designed to best meet the needs of individual management systems. A controlled breeding program should be selected which is appropriate for the existing circumstances and management practices.

Before a controlled breeding program is planned the producer's objectives must be examined and he must be made aware of the projected results and limitations. The producer and his consulting veterinarian should review the operation's breeding history, herd health and nutritional status and agree that a controlled breeding program is practical in the producer's specific situation. For any successful controlled breeding program:

- cows and heifers must be normal, nonpregnant, and cycling (rectal palpation should be performed).
- cattle must be in a fit and thrifty breeding condition and on an adequate or increasing plane of nutrition.
- proper program planning and record keeping are essential.
- if artificial insemination is being used it must be performed by competent inseminators using high quality semen.

It is important to understand that estroPLAN is effective only in animals with a mature corpus luteum (ovulation must have occurred at least 5 days prior to treatment). This must be considered when breeding is intended following a single estroPLAN injection.

### SAFETY AND TOXICITY:

At 50 and 100 times the recommended dose, mild side effects may be detected in some cattle. These include increased uneasiness, slight frothing, and milk let-down.

### CONTRAINDICATIONS:

estroPLAN should not be administered to a pregnant animal whose calf is not to be aborted.

### PRECAUTIONS:

There is no effect on fertility following the single or double dosage regimen when breeding occurs at induced estrus or at 72 and 96 hours post treatment. Conception rates may be lower than expected in those fixed time breeding programs which omit the second insemination (i.e. the insemination at or near 96 hours). This is especially true if a fixed time insemination is used following a single estroPLAN injection.

As with all parenteral products, careful aseptic techniques should be employed to decrease the possibility of post injection bacterial infection. Antibiotic therapy should be employed at the first sign of infection.

### DOSAGE AND ADMINISTRATION:

2ml. of estroPLAN injection (500 mcg of cloprostenol) should be administered by **INTRAMUSCULAR INJECTION** for all indications in both beef and dairy cattle.

### WARNINGS:

For veterinary use only.

Women of child-bearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. In the early stages women may be unaware of their pregnancies.

estroPLAN injection is readily absorbed through the skin and may 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.

### STORAGE CONDITIONS:

1. Protect from light.
2. Store in carton.
3. Store at controlled room temperature 20° - 25°C (68° - 77°F).

### HOW SUPPLIED:

20 mL multidose vials . . . . . NDC 0009-5212-01

### CAUTION:

Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

ANADA 200-310, approved by FDA

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