SYNCHSURE- cloprostenol sodium injection, solution
Boehringer Ingelheim Animal Health USA Inc.

Approved by FDA under ANADA # 200-310

SYNCHSURE®
(cloprostenol injection)

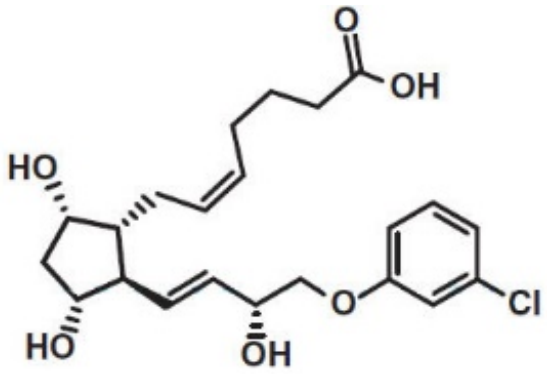
250 mcg cloprostenol/mL (equivalent to 263 mcg cloprostenol sodium/mL)

A sterile solution of a prostaglandin $F_{2\alpha}$ analogue for
intramuscular injection in beef cows, lactating dairy cows,
and replacement beef and dairy heifers

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

DESCRIPTION:

SYNCHSURE® (cloprostenol injection) is a synthetic prostaglandin analogue structurally related to prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$). Each mL of the sterile colorless aqueous solution contains 250 mcg cloprostenol (equivalent to 263 mcg cloprostenol sodium), 5.03 mg sodium citrate, 0.66 mg anhydrous citric acid, 6.76 mg sodium chloride, 1.0 mg chlorocresol, and water for injection, q.s.



INDICATIONS FOR USE:

1. For unobserved or non-detected estrus in beef cows, lactating dairy cows,and replacement beef and dairy heifers

2. For treatment of pyometra or chronic endometritis in beef cows, lactating dairy cows, and replacement beef and dairy heifers

3. For treatment of mummified fetus in beef cows, lactating dairy cows, and replacement beef and dairy heifers

4. For treatment of luteal cysts in beef cows, lactating dairy cows, and replacement beef and dairy heifers

5. For abortion of beef cows, lactating dairy cows, and replacement beef and dairy heifers

6. For estrus synchronization in beef cows, lactating dairy cows, and replacement beef and dairy heifers

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

SYNCHSURE 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.

DOSAGE AND ADMINISTRATION:

Two mL of SYNCHSURE (500 mcg cloprostenol) should be administered by *INTRAMUSCULAR INJECTION* using the specific dosage regimen for the indication.

Discard remaining product 180 days after first use.

1. For unobserved or non-detected estrus in beef cows, lactating dairy cows, and replacement beef and dairy heifers

Cows and heifers which are not detected in estrus, although ovarian cyclicity continues, can be treated with SYNCHSURE 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 estrous detection is not desirable or possible, treated animals may be inseminated twice at about 72 and 96 hours post-injection.

2. For treatment of pyometra or chronic endometritis in beef cows, lactating dairy cows, and replacement beef and dairy heifers

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 SYNCHSURE 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.

3. For treatment of mummified fetus in beef cows, lactating dairy cows, and replacement beef and dairy heifers

Death of the conceptus during gestation may be followed by its degeneration and dehydration. Induction of luteolysis with SYNCHSURE 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.

4. For treatment of luteal cysts in beef cows, lactating dairy cows, and replacement beef and dairy heifers

A cow or heifer 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 SYNCHSURE can restore normal ovarian activity by causing regression of the luteal cyst.

5. For abortion of beef cows, lactating dairy cows, and replacement beef and dairy heifers

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 4 to 5 days after the injection with the reproductive tract returning to normal soon after the abortion. The ability of SYNCHSURE to induce abortion decreases beyond the fifth month of gestation while the risk of dystocia and its consequences increases. SYNCHSURE has not been sufficiently tested under feedlot conditions; therefore recommendations cannot be made for its use in heifers placed in feedlots.

6. For estrus synchronization in beef cows, lactating dairy cows, and replacement beef and dairy heifers

The luteolytic action of SYNCHSURE 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. SYNCHSURE can be used in a breeding program with the following methods:

- Single SYNCHSURE 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 post-injection.
  With a single injection program, it may be desirable to assess the cyclicity status of the herd before SYNCHSURE 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 SYNCHSURE. Breeding should then be continued at the usual time following signs of estrus on the seventh and eighth days. On the ninth and tenth days, 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 days (at about 72 and 96 hours post-injection).
- Double SYNCHSURE 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 SYNCHSURE 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 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 SYNCHSURE to cover any animals returning to estrus.

Management considerations for use of SYNCHSURE for estrus synchronization:
A variety of programs can be designed to best meet the needs of individual management systems. A breeding program should be selected which is appropriate for the existing circumstances and management practices. Before a breeding program is planned, the producer's objectives must be examined and the producer must be made aware of the projected results and limitations. The producer and the consulting veterinarian should review the operation's breeding history, herd health, and nutritional status and agree that a breeding program is practical in the producer's specific situation. For any successful breeding program:

- cows and heifers must be normal, non-pregnant, and cycling (rectal palpation should be performed);
- cows and heifers must be in sound 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 SYNCHSURE 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 SYNCHSURE injection.

There is no difference in the fertility achieved 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 employing SYNCHSURE alone which omit the second insemination (ie, the insemination at or near 96 hours). This is especially true if a fixed time insemination is used following a single SYNCHSURE injection.

7. For use with 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 gonadorelin injection by intramuscular injection on Day 0.
- Administer 2 mL of SYNCHSURE by intramuscular injection 6 to 8 days after the first gonadorelin injection.
- Administer the second gonadorelin injection 30 to 72 hours after the SYNCHSURE injection.

- Perform FTAI 8 to 24 hours after the second gonadorelin injection, or inseminate cows on detected estrus using standard herd practices.

CONTRAINDICATIONS:

Do not use this drug product in pregnant cattle, unless abortion is desired.

WARNINGS AND PRECAUTIONS:

WITHDRAWAL PERIODS AND RESIDUE WARNINGS: No milk discard or pre-slaughter drug withdrawal period is required when used according to labeling. Use of this product in excess of the approved dose may result in drug residues.

USER SAFETY WARNINGS:

Not for use in humans. Keep this and all drugs out of the reach of children.

Women of child-bearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product.

SYNCHSURE 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.

The Safety Data Sheet (SDS) contains more detailed occupational safety information. To obtain an SDS or for technical assistance, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251.

ANIMAL SAFETY WARNINGS:
As with all parenteral products, careful aseptic techniques should be employed to decrease the possibility of post-injection bacterial infection. Severe localized clostridial infections associated with injection of cloprostenol injection have been reported. In rare instances, such infections have resulted in death. Aggressive antibiotic therapy should be employed at the first sign of infection at the injection site,whether localized or diffuse.

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.

CONTACT INFORMATION:

To report suspected adverse drug experiences, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae

HOW SUPPLIED:

100 mL multidose vial

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

See FDA's website http://www.fda.gov/safesharpsdisposal for information on safe disposal of needles and other sharps.

Distributed by:

Boehringer Ingelheim Animal Health USA Inc.
Duluth, GA 30096

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100 mL: 50434-01

1050-8918-03 Rev. 05-2024

PRINCIPAL DISPLAY PANEL - 100 mL Vial

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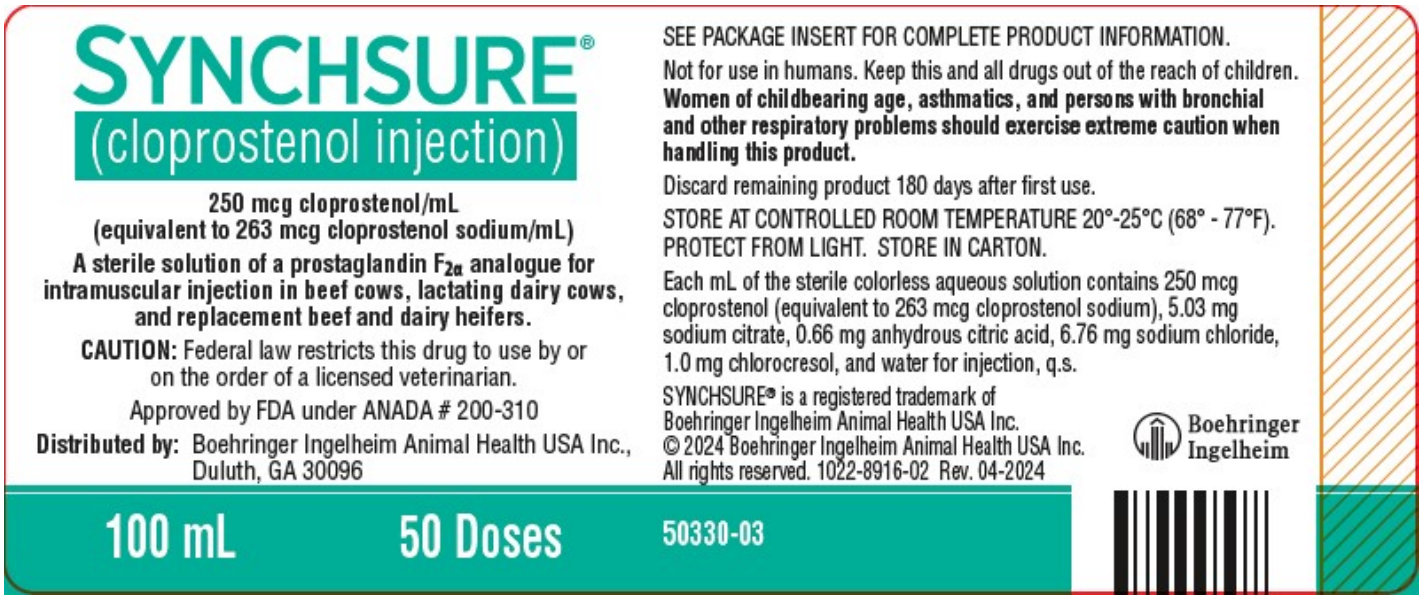
100 mL 50 Doses



SYNCHSURE
cloprostenol sodium injection, solution

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:0010-3549
Route of Administration	INTRAMUSCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
cloprostenol sodium (UNII: 886SAV9675) (cloprostenol - UNII:4208238832)	cloprostenol	250 ug in 1 mL

Inactive Ingredients

Ingredient Name	Strength
CHLOROCRESOL (UNII: 36W53O7109)	1 mg in 1 mL
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	0.66 mg in 1 mL
sodium citrate, unspecified form (UNII: 1Q73Q2JULR)	5.03 mg in 1 mL
sodium chloride (UNII: 451W47IQ8X)	6.76 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0010-3549-01	1 in 1 CARTON		
1		100 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200310	08/10/2021	

Labeler - Boehringer Ingelheim Animal Health USA Inc. (007134091)

Revised: 9/2024 Boehringer Ingelheim Animal Health USA Inc.