American Association of Bovine Practitioners

Prudent Drug Usage Guidelines

The production of safe and wholesome animal products for human consumption is a primary goal of members of the AABP. In reaching that goal, the AABP is committed to the practice of preventive immune system management through the use of vaccines, parasiticides, stress reduction and proper nutritional management. The AABP recognizes that proper and timely management practices can reduce the incidence of disease and therefore reduce the need for antimicrobials; however, antimicrobials remain a necessary tool to manage infectious disease in beef and dairy herds. In order to reduce animal pain and suffering, to protect the economic livelihood of beef and dairy producers, to ensure the continued production of foods of animal origin, and to minimize the shedding of zoonotic bacteria into the environment and potentially the food chain, prudent use of antimicrobials is encouraged. Following are general guidelines for the prudent therapeutic use of antimicrobials in beef and dairy cattle.

1. The veterinarian's primary responsibility to the client is to help design management, immunization, housing and nutritional programs that will reduce the incidence of disease and the need for antimicrobials.

2. Antimicrobials should be used only within the confines of a valid veterinarian-client-patient relationship; this includes both dispensing and issuance of prescriptions.

3. Veterinarians should properly select and use antimicrobial drugs.
   a. Veterinarians should participate in continuing education programs that include therapeutics and emerging and/or development of antimicrobial resistance.
   b. The veterinarian should have strong clinical evidence of the identity of the pathogen causing the disease, based upon clinical signs, history, necropsy examination, laboratory data and past experience.
   c. The antimicrobial selected should be appropriate for the target organism and should be administered at a dosage and route that are likely to achieve effective levels in the target organ.
   d. Product choices and regimens should be based on available laboratory and package insert information, additional data in the literature, and consideration of the pharmacokinetics and pharmacodynamics of the drug.
   e. Antimicrobials should be used with specific clinical outcome(s) in mind, such as fever reduction, return of mastitic milk to normal, or to reduce shedding, contagion and recurrence of disease.
   f. Periodically monitor herd pathogen susceptibility and therapeutic response, especially for routine therapy such as dry cow intramammary antibiotics, to detect changes in microbial susceptibility and to evaluate antimicrobial selections.
   g. Use products that have the narrowest spectrum of activity and known efficacy *in vivo* against the pathogen causing the disease problem.
   h. Antimicrobials should be used at a dosage appropriate for the condition treated for as short a period of time as reasonable, i.e., therapy should be discontinued when it is apparent that the immune system can manage the disease, reduce pathogen shedding and minimize recurrence of clinical disease or development of the carrier state.
   i. Antimicrobials of lesser importance in human medicine should be used in preference to newer generation drugs that may be in the same class as drugs currently used in humans if this can be achieved while protecting the health and safety of the animals.
   j. Antimicrobials labeled for use for treating the condition diagnosed should be used whenever possible. The label, dose, route, frequency and duration should be followed whenever possible.
   k. Antimicrobials should be used extra-label only within the provisions contained within AMDUCA regulations.
   l. Compounding of antimicrobial formulations should be avoided.
   m. When appropriate, local therapy is preferred over systemic therapy.
   n. Treatment of chronic cases or those with a poor chance of recovery should be avoided. Chronic cases should be removed or isolated from the remainder of the herd.
   o. Combination antimicrobial therapy should be discouraged unless there is information to show an increase in efficacy or suppression of resistance development for the target organism.
   p. Prophylactic or metaphylactic use of antimicrobials should be based on a group, source or production unit evaluation rather than being utilized as standard practice.
   q. Drug integrity should be protected through proper handling, storage and observation of the expiration date.

4. Veterinarians should endeavor to ensure proper on-farm drug use.
   a. Prescription or dispensed drug quantities should be appropriate to the production-unit size and expected need so that stockpiling of antimicrobials on the farm is avoided.
   b. The veterinarian should train farm personnel who use antimicrobials on indications, dosages, withdrawal times, route of administration, injection site precautions, storage, handling, record keeping and accurate diagnosis of common diseases. The veterinarian should ensure that labels are accurate to instruct farm personnel on the correct use of antimicrobials.
   c. Veterinarians are encouraged to provide written guidelines to clients whenever possible to describe conditions and instructions for antimicrobial use on the farm or unit.

Presented by the Bacterial Resistance and Prudent Therapeutic Antimicrobial Use Committee. Board approved March 1999.

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LUTALYSE®

brand of dinoprost tromethamine sterile solution

For intramuscular use for estrus synchronization, treatment of unobserved (silent) estrus and pyometra (chronic endometritis) in cattle.

DESCRIPTION

This product contains the naturally occurring prostaglandin F2 alpha (dinoprost) as the tromethamine salt. Each mL contains dinoprost tromethamine equivalent to 5 mg dinoprost: also, benzyl alcohol, 9.45 mg added as preservative. When necessary, pH was adjusted with sodium hydroxide and/or hydrochloric acid. Dinoprost tromethamine is a white or slightly off-white crystalline powder that is readily soluble in water at room temperature in concentrations to at least 200 mg/mL.

INDICATIONS AND INSTRUCTIONS FOR USE

LUTALYSE Sterile Solution is indicated as a luteolytic agent.

LUTALYSE is effective only in those cattle having a corpus luteum, i.e., those which ovulated at least five days prior to treatment. Future reproductive performance of animals that are not cycling will be unaffected by injection of LUTALYSE.

1. **For Intramuscular Use for Estrus Synchronization in Beef Cattle and Non-Lactating Dairy Heifers.** LUTALYSE is used to control the timing of estrus and ovulation in estrous cycling cattle that have a corpus luteum.

   Inject a dose of 5 mL LUTALYSE (25 mg PGF2α) intramuscularly either once or twice at a 10 to 12 day interval.

   With the single injection, cattle should be bred at the usual time relative to estrus.

   With the two injections cattle can be bred after the second injection either at the usual time relative to detected estrus or at about 80 hours after the second injection of LUTALYSE.

   Estrus is expected to occur 1 to 5 days after injection if a corpus luteum was present. Cattle that do not become pregnant to breeding at estrus on days 1 to 5 after injection will be expected to return to estrus in about 18 to 24 days.

2. **For Intramuscular Use for Unobserved (Silent) Estrus in Lactating Dairy Cows with a Corpus Luteum.** Inject a dose of 5 mL LUTALYSE (25 mg PGF2α) intramuscularly. Breed cows as they are detected in estrus. If estrus has not been observed by 80 hours after injection, breed at 80 hours. If the cow returns to estrus breed at the usual time relative to estrus.

3. **For Intramuscular Use for Treatment of Pyometra (chronic endometritis) in Cattle.** Inject a dose of 5 mL LUTALYSE (25 mg PGF2α) intramuscularly. In studies conducted with LUTALYSE, pyometra was defined as presence of a corpus luteum in the ovary and uterine horns containing fluid but not a conceptus based on palpation *per rectum*. Return to normal was defined as evacuation of fluid and return of the uterine horn size to 40mm or less based on palpation *per rectum* at 14 and 28 days. Most cattle that recovered in response to LUTALYSE recovered within 14 days after injection. After 14 days, recovery rate of treated cattle was no different than that of nontreated cattle.

WARNINGS

Not for human use.

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. Dinoprost tromethamine is readily absorbed through the skin and can cause abortion and/or bronchiospasms. Direct contact with the skin should, therefore, be avoided. Accidental spillage on the skin should be washed off **immediately** with soap and water.

Use of this product in excess of the approved dose may result in drug residues.

PRECAUTIONS

Do not administer to pregnant cattle unless abortion is desired.

Do not administer intravenously (I.V.), as this route might potentiate adverse reactions.

Cattle administered a progestogen would be expected to have a reduced response to LUTALYSE Sterile Solution.

Aggressive antibiotic therapy should be employed at the first sign of infection at the injection site whether localized or diffuse. As with all parenteral products careful aseptic techniques should be employed to decrease the possibility of post injection bacterial infections.

ADVERSE REACTIONS

1. The most frequently observed side effect is increased rectal temperature at a 5X or 10X overdose. However, rectal temperature change has been transient in all cases observed and has not been detrimental to the animal.
2. Limited salivation has been reported in some instances.
3. Intravenous administration might increase heart rate.
4. Localized post injection bacterial infections that may become generalized have been reported. In rare instances such infections have terminated fatally. See PRECAUTIONS.

IMPORTANT

No milk discard or preslaughter drug withdrawal period is required for labeled uses.

DOSAGE AND ADMINISTRATION

LUTALYSE Sterile Solution is supplied at a concentration of 5 mg dinoprost per mL. LUTALYSE is luteolytic in cattle at 25 mg (5 mL) administered intramuscularly. As with any multidose vial, practice aseptic techniques in withdrawing each dose. Adequately clean and disinfect the vial closure prior to entry with a sterile needle.

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

Pharmacia & Upjohn Company
Kalamazoo, MI 49001, USA

Revised August 1996
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Micotil® 300 Injection

Tilmicosin Phosphate

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

HUMAN WARNINGS: Not for human use. Injection of this drug in humans may be fatal. Keep out of reach of children. Do not use in automatically powered syringes. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately. Emergency medical telephone numbers are 1-800-722-0987 or 1-317-276-2000. Avoid contact with eyes.

NOTE TO THE PHYSICIAN: The cardiovascular system appears to be the target of toxicity. This antibiotic persists in tissues for several days. The cardiovascular system should be monitored closely and supportive treatment provided. Dobutamine partially offsets the negative inotropic effects induced by Micotil in dogs. β-adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil-induced tachycardia in dogs. Epinephrine potentiated lethality of Micotil in pigs.

For Subcutaneous Use in Cattle Only. Do Not Use in Automatically Powered Syringes.

Indications: Micotil® is indicated for the treatment of bovine respiratory disease (BRD) associated with *Pasteurella haemolytica*. For the control of respiratory disease in cattle at high risk of developing BRD associated with *P. haemolytica*.

Description: Micotil is a solution of the antibiotic tilmicosin. Each mL contains 300 mg of tilmicosin as tilmicosin phosphate in 25% propylene glycol, phosphoric acid as needed to adjust pH and water for injection, q.s. Tilmicosin, USP is produced semi-synthetically and is in the macrolide class of antibiotics.

Actions: Activity — Tilmicosin has an *in vitro** antibacterial spectrum that is predominantly gram-positive with activity against certain gram-negative microorganisms. Activity against several mycoplasma species has also been detected.

Ninety-five percent of the *Pasteurella haemolytica* isolates were inhibited by 3.12 µg/mL or less.

Microorganism	MIC (µg/mL)
Pasteurella haemolytica	3.12
Pasteurella multocida	6.25
Haemophilus somnus	6.25
Mycoplasma dispar	0.097
M. bovirhinis	0.024
M. bovoculi	0.048

*The clinical significance of this *in vitro* data in cattle has not been demonstrated.

Directions — Inject Subcutaneously in Cattle Only. Administer a single subcutaneous dose of 10 mg/kg of body weight (1 mL/30 kg or 1.5 mL per 100 lbs). Do not inject more than 15 mL per injection site.

If no improvement is noted within 48 hours, the diagnosis should be re-evaluated.

Injection under the skin behind the shoulders and over the ribs is suggested.

Note — Swelling at the subcutaneous site of injection may be observed but is transient and usually mild.

CONTRAINDICATION: Do not use in automatically powered syringes. Do not administer intravenously to cattle. Intravenous injection in cattle will be fatal. Do not administer to animals other than cattle. Injection of this antibiotic has been shown to be fatal in swine and non-human primates, and it may be fatal in horses and goats.

CAUTION: Do Not Administer to Swine. Injection in Swine Has Been Shown to be Fatal.

WARNINGS: Animals intended for human consumption must not be slaughtered within 28 days of the last treatment. Do not use in female dairy cattle 20 months of age or older. Use of tilmicosin in this class of cattle may cause milk residues.

CAUTION: The safety of tilmicosin has not been established in pregnant cattle and in animals used for breeding purposes. Intramuscular injection will cause a local reaction which may result in trim loss.

How Supplied: Micotil is supplied in 50 mL, 100 mL and 250 mL multidose amber glass bottles.

Storage: Store at room temperature, 86˚F (30˚C) or below. Protect from direct sunlight.

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Manufactured for Elanco Animal Health
A Division of Eli Lilly and Company
Indianapolis, IN 46285, U.S.A.

AH 0230
NADA 140-929 Approved by FDA
YL00600EAMX

Elanco Animal Health
A Division of Eli Lilly and Company
Four Parkwood
500 E. 96th Street, Suite 125
Indianapolis, Indiana 46240
(800) 428-4441

Micotil® is a trademark for Elanco's brand of tilmicosin.

New bottle. New protective shroud. And still the lowest treatment cost.

Shorter, stouter 250 mL bottle fits more securely in hand...

and features attached Micotil® label for instant access to use and safety information...

while rubber stopper provides a more durable and larger target area.

Reusable shroud is constructed of heavy-duty recyclable clear plastic...

offering enhanced bottle protection, safety and convenient handling...

with an easy-close top, built-in hanger and upright stable positioning from top or bottom.

And still, with all of these new safety and easy handling features,

just one of these newly designed bottles treats thirty-three 500-pound calves — giving you the most cost-effective BRD treatment and control program per head.*

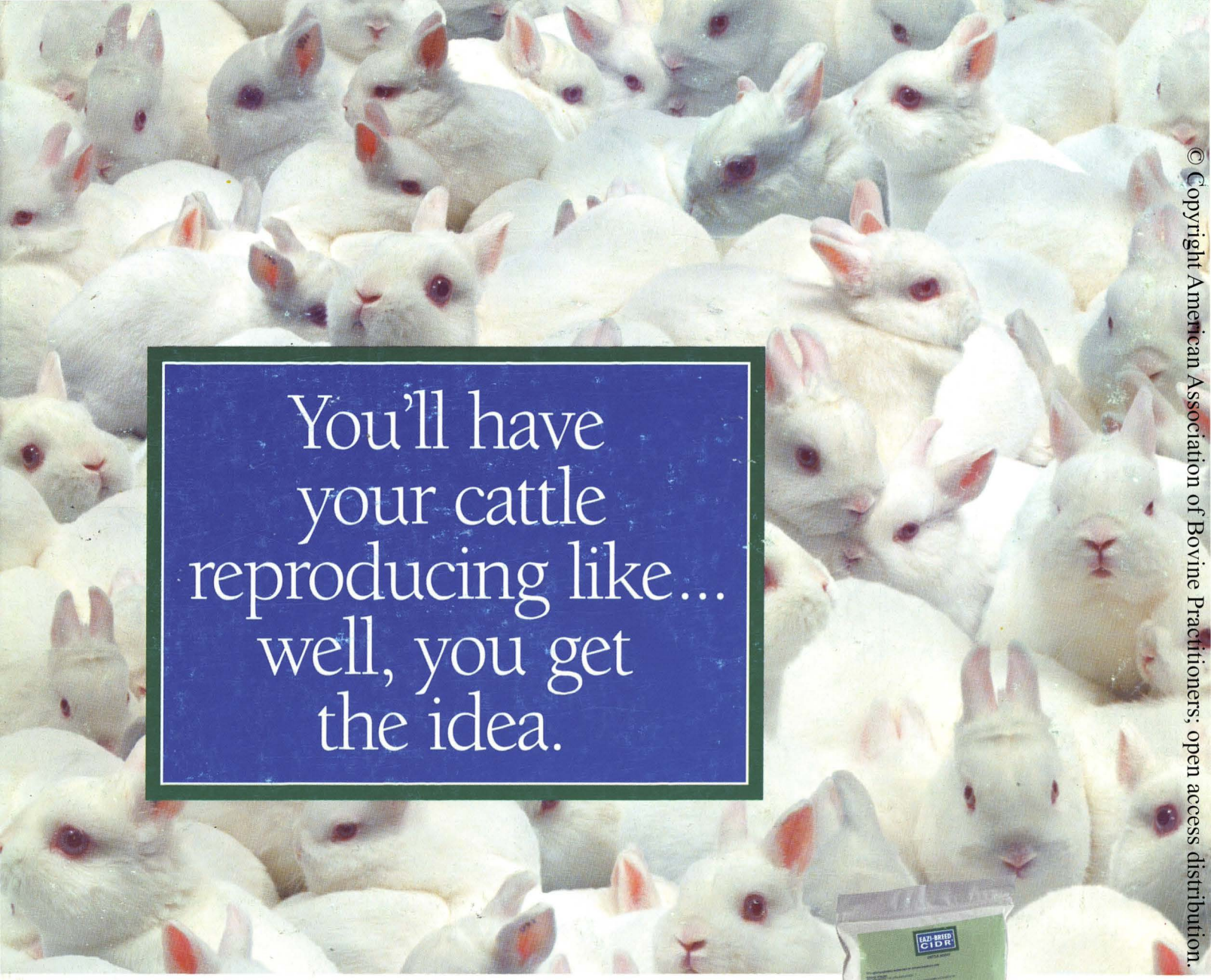
Micotil is to be used by, or on the order of, a licensed veterinarian. Administer subcutaneously to cattle only. Intravenous use in cattle will be fatal. Do not use in female dairy cattle 20 months of age or older. Use in lactating dairy cattle may cause milk residues. See label for complete use information, including human warnings. Always use proper drug handling procedures to avoid accidental self-injection.

ELANCO
Micotil®
TM

TAKE CONTROL

* Based on 500-pound calf; current market price as compared to the combined average treatment cost of Nuflor®, Baytril®, Excenel® and Naxcel®. Market prices may vary.

Micotil® is a trademark for Elanco's brand of tilmicosin.



EAZI-BREED™ CIDR® Cattle Insert improves your beef or dairy heifer breeding program by allowing you to breed more cattle in less time.

Used in breeding programs with LUTALYSE® Sterile Solution (dinoprost tromethamine), EAZI-BREED CIDR:

- Reduces anestrus in beef cattle
- Shortens heat detection time in beef cattle and dairy heifers
- Starts beef heifers cycling earlier

Your results:

- More pregnancies
- More efficient heat detection
- More profit

Ask your Pharmacia Animal Health representative about the EAZI-BREED CIDR Cattle Insert.

When using LUTALYSE, as with all parenteral products, aseptic technique should be used to reduce the possibility of post-injection bacterial infections. Do not administer LUTALYSE in pregnant animals unless cessation of pregnancy is desired. Not for intravenous administration. Women of childbearing age and persons with respiratory problems should exercise extreme caution when handling LUTALYSE.

EAZI-BREED™ CIDR®

Breed More Cattle in Less Time

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PHARMACIA Animal Health