MERCK ANIMAL HEALTH

CATTLE HEALTH PRODUCT PORTFOLIO

MERCK
Animal Health

WHAT DRIVES YOU DRIVES US.

At Merck Animal Health, the science of healthier animals is our way of life. Just as your passion is raising cattle, our passion is boosting your potential by improving cattle health, performance and well-being through innovative science-based solutions.

Your cattle are your livelihood, and we take our commitment to meeting your distinct needs very seriously. That commitment is what drives us to deliver advanced research, product innovations and superior service.

Whether you raise beef or dairy cattle, we offer a complete line of cattle health and performance products for every stage of production. Along with world-class products, we offer technical expertise and solutions that support and complement your business every step of the way.

For more information about Merck Animal Health products and the science of healthier animals, contact your Merck Animal Health representative today.

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RESPIRATORY VACCINES

All Vista® vaccines are labeled for use in pregnant cows and calves nursing pregnant cows. Vista Once, Vista 5 and Vista 3 are the only modified-live vaccines with at least one-year duration of immunity (DOI) label with challenge data for respiratory disease caused by IBR and BVD Type 1 and Type 2. Industry-leading Vista Once and Once PMH® SQ also have a 16-week DOI for *Pasteurella multocida* and *Mannheimia haemolytica*.

Vista Once SQ

For vaccination of healthy cattle using the only avirulent-live culture as an aid in the control of disease caused by *Mannheimia haemolytica* and *Pasteurella multocida*. Aids in the control of disease caused by: Bovine Virus Diarrhea (BVD) Virus (Type 1) Parainfluenza$_3$ (PI_3). Provides modified-live virus vaccine as an aid in the prevention of respiratory disease caused by Infectious Bovine Rhinotracheitis (IBR), BVD Type 2, and Bovine Respiratory Syncytial Virus (BRSV). Additionally, Vista Once SQ is for the vaccination of healthy cows and heifers prior to breeding as an aid in the prevention of fetal infection, including persistently infected calves caused by BVD (Types 1 & 2); and as an aid in the prevention of persistently infected calves caused by BVD (Type 2); and as an aid in the reduction of abortion due to IBR.

10 dose | 50 dose

Vista 5 SQ

For use in healthy cattle as a modified-live virus vaccine as an aid in prevention of disease caused by Infectious Bovine Rhinotracheitis (IBR), Bovine Viral Diarrhea (BVD) Type 2, and Bovine Respiratory Syncytial Virus (BRSV) and as an aid in control of disease caused by BVD Type 1 and Parainfluenza$_3$ (PI_3). In addition, this product is for vaccination of healthy cows and heifers prior to breeding as an aid in reduction of abortion due to IBR and as an aid in prevention of fetal infection, including persistently infected calves caused by BVD (Types 1 & 2). Also available in combination with the only avirulent-live culture as an aid in the control of disease caused by *Mannheimia haemolytica* and *Pasteurella multocida*.

10 dose | 50 dose

Vista 3 SQ

For use in healthy cattle as a modified-live virus vaccine as an aid in the prevention of disease caused by Infectious Bovine Rhinotracheitis (IBR) and Bovine Viral Diarrhea (BVD) Type 2 and as aid in the control of disease caused by BVD Type 1. In addition, this product is for vaccination of healthy cows and heifers prior to breeding as an aid in reduction of abortion due to IBR and as an aid in prevention of fetal infection, including persistently-infected calves caused by BVD Types 1 and 2.

50 dose

RESPIRATORY VACCINES

Once PMH IN

Intranasal bacterial pneumonia vaccine, providing dual protection as an aid in the control of respiratory disease caused by *Mannheimia haemolytica* and as an aid in the prevention of disease caused by *Pasteurella multocida*. Approved for cattle of all ages, starting as young as 1 week of age.

10 dose | 50 dose | 25 x 1 dose

Nasalgen® IP

For the vaccination of healthy cattle as an aid in the prevention of disease caused by IBR and PI_3 virus.

10 dose | 50 dose

Once PMH SQ

As an aid in the control of respiratory disease caused by *Mannheimia haemolytica* and *Pasteurella multocida*.

10 dose | 50 dose

CLOSTRIDIAL VACCINES

Vision® takes the stress out of blackleg protection. Developed to minimize the negative impact of vaccination on performance, Vision offers a high level of immunity with a low level of injection-site reactions. With Vision, you'll see better cost of gains, better feed conversion and greater weaning weights when compared to conventional clostridial vaccines.* Vision is available in a variety of vaccine combinations to fit your needs.

*Take the Stress out of Blackleg Protection (Tech.). (n.d.).

Vision® 7 Somnus

For use in healthy cattle as an aid in preventing disease caused by *Clostridium chauvoei* (Blackleg), *Cl. septicum* (Malignant edema), *Cl. novyi* (Black disease), *Cl. sordellii, Cl. perfringens* Types C and D (Enterotoxemia), and *Haemophilus somnus*.

10 dose | 50 dose | 250 dose

Vision 7

For use in healthy cattle as an aid in preventing disease caused by *Clostridium chauvoei* (Blackleg), *Cl. septicum* (Malignant edema), *Cl. novyi* (Black disease), *Cl. sordellii, and Cl. perfringens* Types C and D (Enterotoxemia).

10 dose | 50 dose | 250 dose

Vision 8 Somnus

For use in healthy cattle as an aid in prevention of disease caused by *Clostridium chauvoei, Cl. septicum, Cl. haemolyticum, Cl. novyi, Cl. sordellii, Cl. perfringens* Types C and D, and *Haemophilus somnus*.

10 dose | 50 dose

Vision 8

For use in healthy cattle as an aid in preventing disease caused by *Clostridium chauvoei* (Blackleg), *Cl. septicum* (Malignant edema), *Cl. haemolyticum* (Bacilliary Hemoglobinuria (Red water)), *Cl. novyi* (Black disease), *Cl. sordellii* and *Cl. perfringens* Types C and D (Enterotoxemia).

10 dose | 50 dose

CLOSTRIDIAL VACCINES CONT.

Vision CD-T

For use in healthy cattle as an aid in preventing disease caused by *Clostridium perfringens* Types C and D (Enterotoxemia) and *Cl. tetani* (Tetanus).

50 dose

Vision CD

For use in healthy cattle as an aid in the prevention of Enterotoxemia caused by *Clostridium perfringens* Types C and D.

250 dose

Cavalry® 9

For the vaccination of healthy cattle as an aid in the prevention of diseases caused by *Clostridium chauvoei*, *Cl. septicum, Cl. novyi* Type B, *Cl. haemolyticum* (known elsewhere as *Cl. novyi* Type D), *Cl. tetani* and *Cl. perfringens* Types C and D.

10 dose | 50 dose | 125 dose

Covexin® 8

For the vaccination of healthy cattle as an aid in the prevention of diseases caused by *Clostridium chauvoei, Cl. septicum, Cl. novyi* Type B, *Cl. haemolyticum* (known elsewhere as *Cl. novyi* Type D), *Cl. tetani* and *Cl. perfringens* Types C and D.

10 dose | 50 dose

SCOURS VACCINES

Minimize calf scour losses with Guardian® and Bovilis® Coronavirus.

Calf scours (neonatal calf diarrhea) continues to be a top cause of calf mortality, and a costly issue for the industry. Guardian delivers superior protection against calf scours by providing neonatal calves with effective clostridium antibodies through vaccination for *E. coli* pilus type K99, Bovine Group A Serotype G6 rotaviruses, Enterotoxemia caused by *Cl. perfringens* Types C and D and Bovine Coronavirus (BCV).

Most severe during winter months, Bovine Coronavirus is often prevalent in dairy calves and cow/calf beef herds, and is frequently diagnosed as the leading pathogen in neonatal calves. Bovilis Coronavirus—the first modified-live, intranasal vaccine available for the reduction of enteric disease caused by coronavirus—is approved for use in calves as young as 3 days of age and can greatly reduce the impact of BCV in the herd.

Guardian

Guardian vaccine is a multiple antigen product that includes a cell-free extract of K99 pilus type of *Escherichia coli*, a unique combination of two inactivated coronaviruses, two G types of inactivated rotaviruses and a bacterin-toxoid from *Clostridium perfringens* Types C and D. It is recommended for use in healthy heifers and cows as an aid in the prevention of neonatal calf diarrhea caused by enterotoxigenic *E. coli* pilus type K99, bovine Group A Serotype G6 rotaviruses, enterotoxemia caused by *Cl. perfringens* Types C and D, and as an aid in the control of neonatal calf diarrhea caused by bovine coronaviruses.

10 dose | 50 dose

Bovilis Coronavirus

For the vaccination of healthy cattle 3 days of age and older as an aid in the reduction of enteric disease caused by Bovine Coronavirus. Safety has been demonstrated in calves 1 day of age or older.

10 dose | 50 dose | 25x1 dose

PINKEYE VACCINES

Stop pinkeye before it starts with Piliguard® vaccines. Piliguard vaccines are designed to help boost immunity against *Moraxella bovis*, the bacteria that causes pinkeye infections. Vaccinating your herd with Piliguard can prevent infections and reduce the severity of infections when outbreaks occur. The Piliguard line includes a variety of formulations, so you can find the option that fits your needs.

Piliguard Pinkeye+7

Aids in the control of pinkeye caused by *Moraxella bovis* strains expressing pili similar to those expressed by isolates referred to by Merck Animal Health as strains EPP 63, FLA 64, and SAH 38, and against diseases caused by *Clostridium chauvoei, Cl. septicum, Cl. novyi* Type B, *Cl. sordellii* and *Cl. perfringens* Types C and D. Immunity is also provided against *Cl. perfringens* Type B. This immunity is derived from the combination of the Type C (beta) and Type D (epsilon) fractions.

10 dose | 50 dose

Piliguard Pinkeye-1 Trivalent

For use in healthy cattle to aid in the control of pinkeye associated with infection by *Moraxella bovis* strains expressing pili similar to those expressed by isolates referred to by Merck Animal Health as Strains EPP 63, FLA 64 and SAH 38.

10 dose | 50 dose

20/20 Vision 7

For use in healthy cattle as an aid in preventing disease caused by *Clostridium chauvoei* (Blackleg), *Cl. septicum* (Malignant edema), *Cl. novyi* (Black disease), *Cl. sordellii* and *Cl. perfringens* Types C and D (Enterotoxemia) and *Moraxella bovis* (Pinkeye or infectious bovine keratoconjunctivitis).

10 dose | 50 dose

NUTRITIONALS

White muscle disease can be devastating to your herd, especially in young calves. Treat and prevent white muscle disease with BO-SE® (selenium and d-alpha-tocopherol acetate). Gentle but effective, BO-SE is formulated just for calves.

Is your herd at risk for Selenium-Tocopherol Deficiency? Ask your veterinarian about MU-SE® (selenium and d-alpha-tocopherol acetate). The injectable solution combines selenium and vitamin E to treat and prevent Selenium-Tocopherol Deficiency in calves and breeding cows.

BO-SE (selenium, vitamin E) Injection

Emulsion of selenium-tocopherol for the prevention and treatment of white muscle disease (Selenium-Tocopherol Deficiency) syndrome in calves.[1]

100 mL

MU-SE (selenium, vitamin E) Injection

Emulsion of selenium-tocopherol for the prevention and treatment of white muscle disease (Selenium-Tocopherol Deficiency) syndrome in calves and as an aid in the prevention and treatment of Selenium-Tocopherol Deficiency in pregnant cows. Approved for weanling calves and breeding beef cows.[2]

100 mL

BO-SE (selenium, vitamin E) Injection

Important safety information on BO-SE (selenium, vitamin E)
Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Contraindications: DO NOT USE IN PREGNANT EWES. Deaths and abortions have been reported in pregnant ewes injected with this product.

Warnings: Anaphylactoid reactions, some of which have been fatal, have been reported in animals administered BO-SE Injection. Signs include excitement, sweating, trembling, ataxia, respiratory distress and cardiac dysfunction. Discontinue use 30 days before the treated calves are slaughtered for human consumption. Selenium -Vitamin E preparations can be toxic when improperly administered.

Precautions: Selenium-Tocopherol Deficiency (STD) syndrome produces a variety and complexity of symptoms often interfering with proper diagnosis. Even in selenium deficient areas there are other disease conditions which produce similar clinical signs. It is imperative that all these conditions are carefully considered prior to the treatment of STD syndrome. Serum selenium levels, elevated SGOT, and creatine serum levels may serve as aids in arriving at a diagnosis of STD, when associated with other indices. Selenium is toxic if administered in excess. A fixed dose schedule is therefore important (read the package insert for each selenium-tocopherol product carefully before using).
Important: Use only the selenium-tocopherol product recommended for each species. Each formulation is designed for the species indicated to produce the maximum efficacy and safety.

Adverse Reactions: Reactions, including acute respiratory distress, frothing from the nose and mouth, bloating, severe depression, abortion and deaths have occurred in pregnant ewes. No known treatment exists because at this time the cause of the reaction is unknown.

For complete information on use refer to product package insert on page 54.

[1] For complete information on BO-SE use, contraindications, warnings and adverse reactions, page 54.

MU-SE (selenium, vitamin E) Injection (100 mL)

Important safety information on MU-SE (selenium, vitamin E)
Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Contraindications: Do not use in adult dairy cattle. Premature births and abortions have been reported in dairy cattle injected with this product during the third trimester of pregnancy. Anaphylactoid reactions, some of which have been fatal, have been reported in cattle administered the MU-SE product. Signs include excitement, sweating, trembling, ataxia, respiratory distress, and cardiac dysfunction. Use only as directed in weanling calves and breeding beef cows. Discontinue use 30 days before the treated cattle are slaughtered for human consumption.

Caution: Selenium is toxic if administered in excess. A fixed dose schedule is therefore important (read package insert for each selenium-tocopherol product carefully before using).

Precautions: Selenium-Tocopherol Deficiency (STD) syndrome produces a variety and complexity of symptoms often interfering with proper diagnosis. Even in selenium deficient areas there are other disease conditions which produce similar clinical signs. It is imperative that all these conditions are carefully considered prior to the treatment of STD syndrome. Serum selenium levels, elevated SGOT, and creatine serum levels may serve as aids in arriving at a diagnosis of STD, when associated with other indices.

Important: Use only the selenium-tocopherol product recommended for each species. Each formulation is designed for the species indicated to produce the maximum efficacy and safety.

For complete information on use refer to product package insert on page 54.

[2] For complete information on MU-SE use, contraindications, warnings and adverse reactions, page 54.

ANTI-INFECTIVES/THERAPEUTICS

Bovine Respiratory Disease (BRD) is a multi-factorial disease. Even though it has been studied extensively, BRD still remains the number one cause of disease and death in cattle. Our anti-infective/therapeutic lineup provides fast-acting control and treatment of BRD.

Zuprevo® 18% (tildipirosin)

Indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida*, and *Histophilus somni* in beef and non-lactating dairy cattle, and for the control of respiratory disease in beef and non-lactating dairy cattle at high risk of developing BRD associated with *M. haemolytica, P. multocida*, and *H. somni*.[1]

100 mL | 250 mL

Resflor Gold® (florfenicol and flunixin meglumine)

Indicated for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni, Mycoplasma bovis*, and control of BRD-associated pyrexia in beef and non-lactating dairy cattle.[2]

100 mL | 250 mL | 500 mL

Nuflor® (florfenicol) Injectable Solution

Indicated for treatment of bovine respiratory disease (BRD), associated with *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni* (Haemophilus somnus), and for the treatment of bovine interdigital phlegmon (foot rot, acute interdigital necrobacillosis, infectious pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*. Also, indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni* (Haemophilus somnus).[3]

100 mL | 250 mL | 500 mL

Banamine® (flunixin meglumine) Injectable Solution

Indicated for the control of pyrexia associated with bovine respiratory disease, endotoxemia and acute bovine mastitis. Also indicated for the control of inflammation in endotoxemia.[4]

100 mL | 250 mL

ANTI-INFECTIVES/THERAPEUTICS
IMPORTANT SAFETY INFORMATION

Banamine® Transdermal (flunixin transdermal solution)

Indicated for the control of pain associated with foot rot and the control of pyrexia associated with bovine respiratory disease (BRD). It is a non-steroidal anti-inflammatory drug (NSAID), and the first non-parasiticide cattle product to be administered as a pour-on.

100 mL | 250 mL | 1 L

Zuprevo 18% (tildipirosin)

IMPORTANT SAFETY INFORMATION: FOR USE IN ANIMALS ONLY. NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. TO AVOID ACCIDENTAL INJECTION, DO NOT USE IN AUTOMATICALLY POWERED SYRINGES WHICH HAVE NO ADDITIONAL PROTECTION SYSTEM. IN CASE OF HUMAN INJECTION, SEEK MEDICAL ADVICE IMMEDIATELY AND SHOW THE PACKAGE INSERT OR LABEL TO THE PHYSICIAN. DO NOT USE Zuprevo 18% IN SWINE. Fatal adverse events have been reported following the use of tildipirosin in swine. NOT FOR USE IN CHICKENS OR TURKEYS. Cattle intended for human consumption must not be slaughtered within 21 days of the last treatment. Do not use in female dairy cattle 20 months of age or older. Use of this drug product in these cattle may cause milk residues. A withdrawal period has not been established in pre-ruminating calves. Do not use in calves to be processed for veal. The effects of Zuprevo 18% on bovine reproductive performance, pregnancy and lactation have not been determined. Swelling and inflammation, which may be severe, may be seen at the injection site after administration. Subcutaneous injection may result in local tissue reactions which persist beyond slaughter withdrawal period. This may result in trim loss of edible tissue at slaughter.

[1]For complete information on Zuprevo use, contraindications, warnings and adverse reactions, see page 55.

Resflor Gold (florfenicol and flunixin meglumine)

IMPORTANT SAFETY INFORMATION: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains material that can be irritating to skin and eyes. Animals intended for human consumption must not be slaughtered within 38 days treatment. This product is not approved for use in female dairy cattle 20 months of age or older, including dry dairy cows. Use in these cattle may cause drug residues in milk and/or in calves born to these cows. A withdrawal period has not been established in pre-ruminating calves. Do not use in calves to be processed for veal. Do not use in animals that have shown hypersensitivity to florfenicol or flunixin. Not for use in animals intended for breeding purposes. The effects of florfenicol and flunixin on bovine reproductive performance, pregnancy, and lactation have not been determined. When administered according to the label directions, Resflor Gold may induce a transient local reaction in the subcutaneous and underlying muscle tissue.

[2]For complete information on Resflor Gold use, contraindications, warnings and adverse reactions, see page 48.

Nuflor (florfenicol) Injectable Solution:

IMPORTANT SAFETY INFORMATION: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains materials that can be irritating to skin and eyes.
RESIDUE WARNINGS: Animals intended for human consumption must not be slaughtered within 28 days of the last intramuscular treatment.
Animals intended for human consumption must not be slaughtered within 38 days of subcutaneous treatment. Do not use in female dairy cattle 20 months of age or older. Use of florfenicol in this class of cattle may cause milk residues. A withdrawal period has not been established in preruminating calves. Do not use in calves to be processed for veal. Not for use in animals intended for breeding purposes. The effects of florfenicol on bovine reproductive performance, pregnancy, and lactation have not been determined. Intramuscular injection may result in local tissue reaction which persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe.

[3]For complete information on Resflor Gold use, contraindications, warnings and adverse reactions, see page 49.

Banamine (flunixin meglumine) Injectable Solution:

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Milk that has been taken during treatment and for 36 hours after the last treatment must not be used for food. Not for use in dry dairy cows. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. Not for use in horses intended for food. Approved only for intravenous administration in cattle. Intramuscular administration has resulted in violative residues in the edible tissues of cattle sent to slaughter.

[4]For complete information on Banamine use, contraindications, warnings and adverse reactions, see page 50.

Banamine® Transdermal (flunixin transdermal solution)

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 8 days of the last treatment. Not for use in female dairy cattle 20 months of age or older, including dry dairy cows; use in these cattle may cause drug residues in milk and/or in calves born to these cows or heifers. Not for use in suckling beef calves, dairy calves, and veal calves. A withdrawal period has not been established for this product in pre-ruminating calves

[4]For complete information on Banamine Transdermal use, contraindications, warnings and adverse reactions, see page 51.

UDDER HEALTH

Good udder health contributes to the wellness of dairy cattle. It also helps dairy farmers save costs and achieve better milk quality and production. Merck Animal Health offers treatment and prevention solutions to maintain quality in every drop of milk.

Orbenin®-DC (benzathine cloxacillin) Intramammary Infusion

For the treatment and prophylaxis of bovine mastitis in non-lactating cows due to *Staphylococcus aureus* and *Streptococcus agalactiae*.[5]

12 dose

Amoxi-Mast® (amoxicillin) Intramammary Antibiotic

An intramammary preparation containing amoxicillin for the treatment of subclinical infectious bovine mastitis in lactating cows due to *Streptococcus agalactiae* and penicillin-sensitive *Staphylococcus aureus*.[6]

12 dose

Dariclox® (sodium cloxacillin) Intramammary Antibiotic

For the treatment of bovine mastitis in lactating cows due to *Streptococcus agalactiae* and nonpenicillinase-producing *Staphylococcus aureus*.[7]

12 dose

Bovilis J-5

For the vaccination of healthy dairy cattle as an aid in the reduction of mastitis due to *Escherichia coli*.

50 dose

[5] For complete information about Orbenin-DC use, contraindications, warnings and adverse reactions, see page 51.
[6] For complete information about Amoxi-Mast use, contraindications, warnings and adverse reactions, see page 51.
[7] For complete information about Dariclox use, contraindications, warnings and adverse reactions, see page 52.

UDDER HEALTH
IMPORTANT SAFETY INFORMATION

Orbenin-DC (benzathine cloxacillin) Intramammary Infusion:

WARNINGS: For use in dry cows only. Do not use within four weeks (28 days) of calving. Treated animals must not be slaughtered for food purposes within four weeks (28 days) of treatment. For complete information about Orbenin-DC use, contraindications, warnings and adverse reactions, see page 51.

Amoxi-Mast (amoxicillin) Intramammary Antibiotic:

WARNINGS: Milk taken from animals during treatment and for 60 hours (five milkings) after the last treatment must not be used for food. Treated animals must not be slaughtered for food purposes within 12 days after the last treatment. For more information, see the product label.

Dariclox (sodium cloxacillin) Intramammary Antibiotic:

WARNINGS: Milk taken from animals during treatment and for 48 hours (four milkings) after the last treatment must not be used for food. Treated animals must not be slaughtered for food purposes within 10 days after the last treatment. For more information, see the product label.

REPRODUCTION

Reproductive performance is a major factor affecting the production and economic efficiency of cattle operations. Let our powerful lineup of reproductive products help you improve your overall herd health and increase your bottom line.

Estrumate® (cloprostenol sodium)

Prostaglandin analogue containing cloprostenol sodium used to induce luteolysis in dairy cattle.[1]

10 dose | 50 dose

Fertagyl® (gonadorelin)

Indicated for the treatment of ovarian follicular cysts in dairy cattle. Also for use with Estrumate (cloprostenol sodium) to synchronize estrous cycles to allow for fixed time artificial insemination in lactating dairy cows.[2]

10 dose | 50 dose

CHORULON® (chorionic gonadotropin)

Indicated for use in dairy cows for the treatment of nymphomania (frequent or constant heat) due to cystic ovaries.[3]

5 dose

Vista 3 VL5 SQ

For the vaccination of healthy cows and heifers prior to breeding as an aid in the reduction of abortion due to IBR; and as an aid in the prevention of fetal infection, including persistently infected calves caused by BVD virus Type 1 and Type 2. In addition, it can be used as an aid in the prevention of disease caused by IBR, BVD Type 2; as an aid in the control of disease caused by BVD Type 1; as an aid in reducing infertility (reproductive disease caused by *Campylobacter fetus*); and as an aid in preventing leptospirosis and as an aid in prevention of urinary shedding of *L. hardjo* organisms.

10 dose | 50 dose

REPRODUCTION CONT.

Vista 5 L5 SQ

For vaccination of healthy cows, using the one of the only one-dose *Leptospira hardjo-bovis* protection in combination with five-way, modified-live virus as an aid in the reduction of abortion due to Infectious Bovine Rhinotracheitis (IBR); as an aid in prevention of fetal infection, including persistently infected calves caused by Bovine Viral Diarrhea (BVD) Type 1 and Type 2. In addition, it can be used as an aid in prevention of disease caused by IBR, BVD Type 2 and Bovine Respiratory Syncytial Virus (BRSV); as an aid in the control of disease caused by BVD Type 1 and Parainfluenza$_3$ (PI$_3$); and as an aid in preventing Leptospirosis and as an aid in prevention of urinary shedding of *L. hardjo* organisms.

10 dose | 50 dose

Vista 5 VL5 SQ

For vaccination of healthy cows, using five-way, modified-live virus as an aid in the reduction of abortion due to Infectious Bovine Rhinotracheitis (IBR); as an aid in the prevention of fetal infection, including persistently infected calves caused by Bovine Viral Diarrhea (BVD) Type 1 and Type 2. In addition, it can be used as an aid in the prevention of disease caused by IBR, BVD (Type 2), and bovine respiratory syncytial virus (BRSV); as an aid in the control of disease caused by BVD (Type 1), and Parainfluenza$_3$ virus (PI$_3$); as an aid in reducing infertility (reproductive disease caused by *Campylobacter fetus*). Features five-way Leptospira protection as an aid in preventing leptospirosis and as an aid in prevention of urinary shedding of *L. hardjo* organisms.

10 dose | 50 dose

L5 SQ

For use in vaccination of healthy cattle as an aid in preventing Leptospirosis including *L. borgpetersenii* serovar *hardjo bovis*; and as an aid in prevention of urinary shedding of *L. hardjo* organisms.

50 dose

VL5 SQ

For use in vaccination of healthy cattle as an aid in reducing infertility (reproductive disease caused by *Campylobacter fetus*); and as an aid in preventing Leptospirosis including *L. borgpetersenii* serovar *hardjo bovis;* and as an aid in prevention of urinary shedding of *L. hardjo* organisms.

50 dose

REPRODUCTION IMPORTANT SAFETY INFORMATION

Important safety information on Estrumate

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 pregnant animal whose calf is not to be aborted. For complete information on use refer to product package insert on page 52.

Warnings: For veterinary use only. Women of childbearing 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.

For complete information on use refer to product package insert on page 52.

[1] For complete information on Estrumate use, contraindications, warnings and adverse reactions, see page 52.

Important safety information on Fertagyl

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian. For complete information on use refer to product package insert on page 51.

[2] For complete information on Fertagyl use, contraindications, warnings and adverse reactions, see page 52.

Important safety information on Chorulon

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.
Adverse Reactions: Chorionic gonadotropin is a protein. In the unlikely event of an anaphylactic reaction, epinephrine should be administered. The administration of an antihistamine may also be indicated.

Residue Warnings: No withdrawal period is required for cows treated according to label directions. For complete information on use refer to product package insert on page 53.

[3] For complete information on Chorulon use, contraindications, warnings and adverse reactions, see page 53.

IMPLANTS – FEEDYARD CATTLE

Reliable, safe and effective. That's why you can count on Revalor® (trenbolone acetate and estradiol).

The Merck Animal Health portfolio of cattle implants—including Revalor and Finaplix® (trenbolone acetate)—helps cattle feeders find the optimal balance between quality and efficiency. Packaged in 10-pellet cartridges, there's an implant to fit every feeding scenario at your operation.

A withdrawal period has not been established for Ralgro, Revalor and Finaplix in pre-ruminating calves. Do not use in calves to be processed for veal. For complete information, refer to the product label.

Revalor-XS (trenbolone acetate and estradiol)

Revalor-XS is an implant containing 200 mg of trenbolone acetate and 40 mg of estradiol. It is designed for steers fed in confinement and provides two doses in one single implant. The first dose, designed to be given when cattle are processed, is effective immediately, while the second dose, shielded by patented X7™ polymer coating, goes to work 70 to 80 days later without the need to re-process the cattle. Each implant consists of 10 small yellow pellets and each cartridge contains 10 implants.

10 x 10

Revalor-XH (trenbolone acetate and estradiol)

Revalor-XH is an implant containing 200 mg of trenbolone acetate and 20 mg of estradiol. It is designed for heifers fed in confinement and provides two doses in one single implant. The first dose, designed to be given when cattle are processed, is effective immediately, while the second dose, shielded by patented X7™ polymer coating, goes to work 70 to 80 days later without the need to re-process the cattle. Each implant consists of 10 small yellow pellets and each cartridge contains 10 implants.

10 x 10

Revalor-200 (trenbolone acetate and estradiol)

Revalor-200 is an implant containing 200 mg of trenbolone acetate and 20 mg estradiol. This product is used in an aggressive implant strategy as a single implant in confined cattle on feed for up to 130 days, or as a terminal implant in a re-implant strategy for steers and heifers fed for more than 130 days. This product is designed with a slow-release delivery system, which increases rate of weight gain and improves feed efficiency in steers and heifers fed in confinement. Each implant consists of 10 small yellow pellets. Ten implants are provided in each cartridge.

10 x 10

Revalor-IS (trenbolone acetate and estradiol)

Revalor-IS is an implant containing 80 mg of trenbolone acetate and 16 mg estradiol. This original implant is intended to be used in short-term confined cattle and is designed with a slow-release delivery system for better quality grade. Each implant consists of four small yellow pellets and 10 implants are enclosed in each cartridge.

10 x 10

IMPLANTS – FEEDYARD CATTLE CONT.

A withdrawal period has not been established for Ralgro, Revalor and Finaplix in pre-ruminating calves. Do not use in calves to be processed for veal. For complete information, refer to the product label.

Revalor-IH (trenbolone acetate and estradiol)

Revalor-IH is an implant containing 80 mg of trenbolone acetate and 8 mg estradiol. This original implant is intended for use as an initial implant in a re-implant strategy for heifers fed in confinement for more than 130 days. Each slow-release implant consists of four small yellow pellets and each cartridge contains 10 implants.

10 x 10

Revalor-S (trenbolone acetate and estradiol)

Revalor-S is the original implant containing 120 mg of trenbolone acetate and 24 mg of estradiol. It is intended for confined steers as a single implant for steers being fed for less than 130 days. Revalor-S increases rate of weight gain and improves feed efficiency in a slow-release delivery system. Each implant consists of six small yellow pellets. Ten implants are enclosed in each cartridge.

10 x 10

Revalor-H (trenbolone acetate and estradiol)

Revalor-H is the original implant containing 140 mg of trenbolone acetate and 14 mg estradiol. It is intended to be used as a single implant for confined heifers fed for less than 130, or as a terminal implant in an implant strategy for confined heifers fed for more than 130 days. Revalor-H increases rate of weight gain and improves feed efficiency in a slow-release delivery system. Each implant consists of seven small yellow pellets. Ten implants are enclosed in each cartridge.

10 x 10

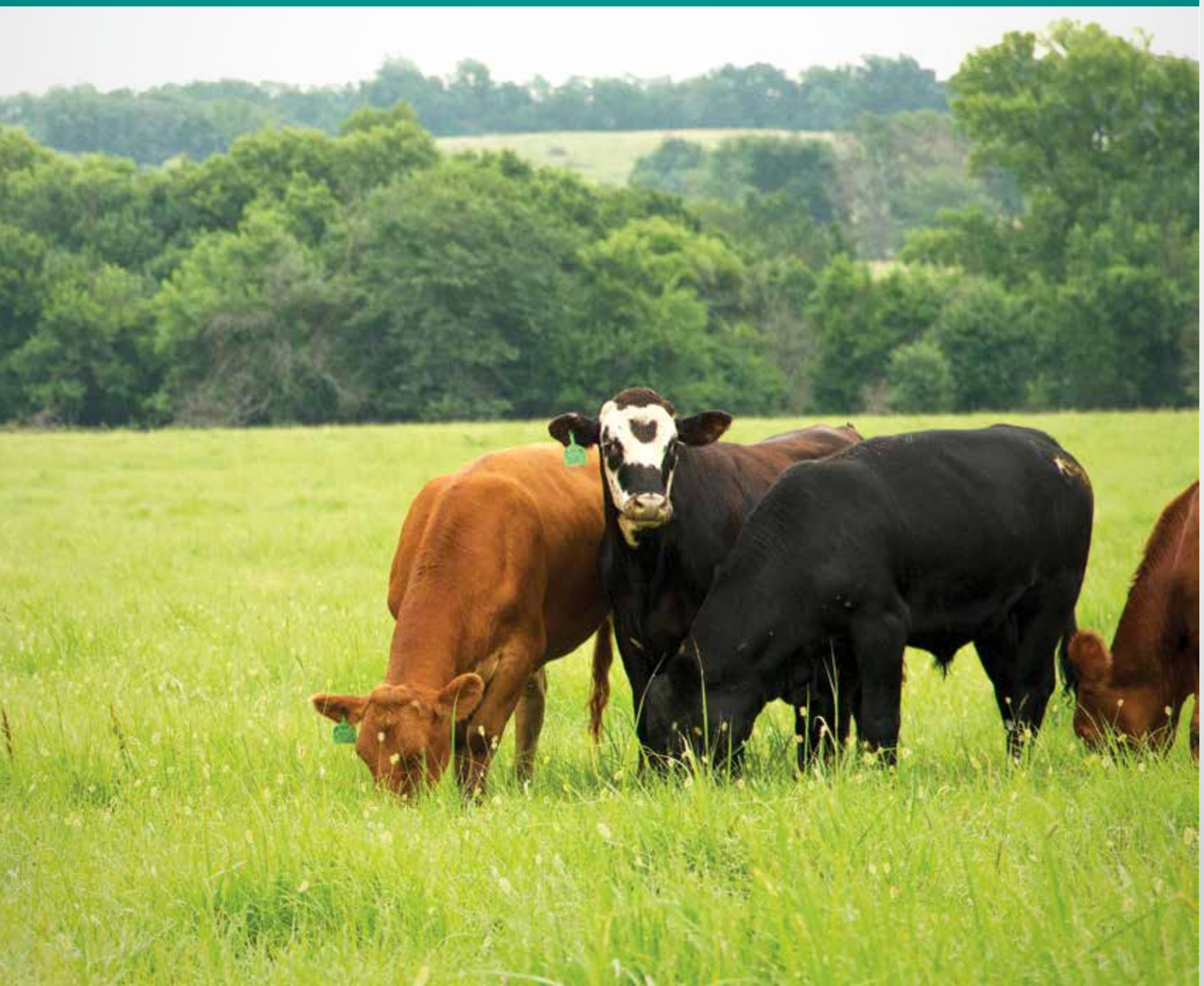
Finaplix-H (trenbolone acetate)

Finaplix-H is a non-generic implant containing 200 mg of trenbolone acetate. It is intended for use in feedlot heifers 90 to 100 days prior to harvest. Finaplix-H provides optimum performance with relatively little risk of quality grade decline when feeding melengestrol acetate. Each implant consists of 10 small yellow pellets, and each pellet contains 20 mg of trenbolone acetate. There are 10 Finaplix-H implants provided in a cartridge.

10 x 10

IMPLANTS – PASTURE CATTLE

From suckling beef calves to weaned pasture steers and heifers, Merck Animal Health has a pasture implant solution to fit your operation's needs. Ralgro® (zeranol) stimulates animals' own natural growth systems to increase weight of gain. Revalor-G uses a lower hormone dosage, designed specifically for stocker cattle on pasture.



A withdrawal period has not been established for Ralgro, Revalor and Finaplix in pre-ruminating calves. Do not use in calves to be processed for veal. For complete information, refer to the product label.

Ralgro (zeranol)

Increases rate of weight gain of suckling beef calves. It also increases the rate of weight gain and improves feed conversion of weaned beef calves, growing beef cattle, feedlot steers and feedlot heifers. The active ingredient zeranol stimulates the animal's own natural growth system. Each implant contains three pellets of 12 mg zeranol totaling 36 mg per implant. There are 24 Ralgro implants provided in a cartridge.

1 x 24 | 10 x 24

Revalor-G (trenbolone acetate and estradiol)

Revalor-G is an implant containing 40 mg of trenbolone acetate and 8 mg estradiol. It is intended for use in weaned pasture steers and heifers. Revalor-G uses a lower hormone dosage, designed for stocker cattle on pasture. Each implant consists of two small yellow pellets. Ten implants are enclosed in each cartridge.

2 x 10 | 10 x 10

PARASITE CONTROL — INTERNAL

Internal parasite control is the cornerstone of an effective animal health program. Powered by fenbendazole, Safe-Guard® (fenbendazole) and Panacur® (fenbendazole) work differently than macrocyclic lactones, which have resistance issues due to overuse.* Safe and proven to work fast, they go straight to the gut, killing the worms where they live, ultimately reducing pasture contamination. Available in drench, paste, and a wide variety of non-handling formulations. The non-handling forms provide all the benefits of an effective deworming without all the labor, handling and stress.

*Bliss, D. H., Ph.D. (2008). Parasite Resistance in US Cattle. The AABP Proceedings, 41, 109-114. Retrieved September 21, 2017.

Safe-Guard (fenbendazole) Suspension (Drench)

A single application, low-dose volume suspension with easy-to-use applicator gun for accurate, stress-free deworming. One liter deworms 43,478 lb. of cattle; one gallon deworms 164,565 lb. 10 liters deworms 434,780 lb. of cattle. (2.3mL/100 lb. of cattle).[1]

10 Liter | Liter | Gallon

Safe-Guard (fenbendazole) Paste

A single application, low-dose volume paste with specially designed metal hook for convenient dosing. Each 290 g paste cartridge deworms 12,100 lb. of cattle.[1]

290 g paste cartridge

Safe-Guard (fenbendazole) En-Pro-AL® Molasses Block

Comes in highly palatable, 25 lb. block of En-Pro-AL® soft-poured molasses. One block treats 8,000 lb. (500 lb. of cattle per 1.5 lb.).[2]

25 lb. block

Safe-Guard (fenbendazole) Protein Block

Comes in highly palatable, 25 lb., 20% protein block. One block treats 8,000 lb. (500 lb. of cattle per 1.5 lb.).[3]

25 lb. block

PARASITE CONTROL - INTERNAL CONT.

Safe-Guard (fenbendazole) Free-Choice Mineral
Available in a 25 lb. plastic pail of 20% salt and is the only dewormer available in a free-choice mineral form. Feed over a three- to six-day period; 8 oz. per 500 lb. of cattle.[4]

25 lb. pail

Safe-Guard (fenbendazole) Alfalfa-Based Pellets
Available in 10 lb. bags of 0.5% (fenbendazole) Alfalfa-based pellets. One pound deworms 1,000 lb. of cattle.[4]

10 lb. bag

Safe-Guard (fenbendazole) Liquid Feed
The first and only FDA-approved complete liquid feed dewormer on the market. Cattle can now get the parasite protection they require on-pasture on a free-choice basis any time in a highly palatable formulation. The standardized free-choice liquid feed delivers the necessary dose of fenbendazole in an average of three to six days, which is needed to keep both your cattle and your bottom line healthy.[4]

PANACUR (fenbendazole) Suspension (Drench)
Available from your veterinarian. For removal and control of Lungworms, Stomach worms (Barberpole worms, brown stomach worms, small stomach worms) and Intestinal worms (Hookworms, thread-necked intestinal worms, small intestinal worms, bankrupt worms and nodular worms).[1] Read full product insert on page 52.

Liter | Gallon

Additional non-handling dewormers featuring Safe-Guard are available through authorized feed manufacturers and distributors in multiple forms and concentrations, including: pellets, meal, mineral and range cubes. Formulations and concentrations may vary by company so follow label directions for use. Contact your animal health representative for more information.

Consult your local veterinarian for assistance in the diagnosis, treatment and control of parasitism.

[1] Safe-Guard drench and paste:

RESIDUE WARNING: Cattle must not be slaughtered within eight days following last treatment. For dairy cattle, the milk discard time is zero hours. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

[2] Safe-Guard EN-PRO-AL Molasses Block:

RESIDUE WARNING: Cattle must not be slaughtered within 11 days following last treatment. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal.

[3] Safe-Guard Protein Block:

RESIDUE WARNING: Cattle must not be slaughtered within 16 days following last treatment. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal.

[4] Safe-Guard mineral, feed through products and liquid feed:

RESIDUE WARNING: Cattle must not be slaughtered within 13 days following last treatment. For dairy cattle, the milk discard time is zero hours. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

*Data on file

PARASITE CONTROL — EXTERNAL

External parasites – such as lice, mites and flies – present a year-round challenge to cattle and handlers. By controlling these nuisances, producers can increase cattle performance and well-being, and also help reduce the spread of diseases. Since external parasites can vary from operation to operation and by geography, Merck Animal Health provides a variety of external parasite control products to adapt to the needs of the location.

Ultra Saber™ Pour-On

1% Lambdacyhalothrin, 5% Piperonyl Butoxide

Provides fast, long-lasting control of horn flies and lice. Applied in a convenient low-dose application – 10 mL for animals 600 lb. or less, and 15 mL for animals more than 600 lb.

Gallon | 900 mL

Saber™ Pour-On

1% Lambdacyhalothrin

Provides fast, long-lasting control of horn flies and lice. Applied in a convenient low-dose application – 10 mL for animals 600 lb. or less, and 15 mL for animals more than 600 lb.

Gallon | 900 mL

Synergized DeLice® Pour-On Insecticide

1% Permethrin, 1% Piperonyl Butoxide

Controls lice, horn flies and face flies on lactating and non-lactating cattle. Also approved for use in backrubbers.

Gallon

Ultra Boss® Pour-On Insecticide

5% Permethrin and 5% Piperonyl Butoxide

A pour-on insecticide for beef, dairy, and lactating cattle. Low-volume dosage reduces time and labor. No preslaughter withdrawal. No milk discard. Target species: lice, horn flies, face flies, horse flies, stable flies, mosquitoes, black flies and ticks. Apply 3 mL per 100 lb. body weight, up to the 30 mL maximum application limit. Also approved for use in backrubbers.

Gallon | Quart

PARASITE CONTROL - EXTERNAL CONT.

Boss® Pour-On Insecticide

5% Permethrin

Pour-on horn fly, face fly and lice control for lactating and non-lactating cattle. Low-volume, no preslaughter withdrawal, no milk discard. Apply 3 mL per 100 lb. body weight, up to the 30 mL maximum application limit.

Gallon | Quart

Grenade® ER

9.7% Lambdacyhalothrin

A broad-spectrum premise insecticide for pest control in, on and around livestock buildings, structures and surroundings. Microencapuslated for long-lasting control of a wide variety of insects that plague surfaces.

8 oz.

ATROBAN® 11% EC

11% Permethrin Emulsifiable Concentrate

Controls horn flies, face flies, stable flies, house flies, horse flies, black flies, mosquitoes, eye gnats, mites, ticks and lice.

Quart | Pint

Double Barrel® VP

14% Pirimiphos Methyl and 6.8% Lambdacyhalothrin

Two active ingredients minimize development of resistance. Up to five months control of horn flies and face flies on non-lactating cattle and calves.

20 ear tags per box

Saber™ Extra Insecticide Ear Tags

10% Lambdacyhalothrin and 13% Piperonyl Butoxide

For up to five-months control of horn flies and up to four-months control of face flies on beef cattle and calves.

20 ear tags per box

Dominator® Insecticide Ear Tags

20% Pirimiphos Methyl

Controls horn flies for up to five months (including synthetic pyrethroidresistant horn flies) and as an aid in the control of face flies on beef. Twenty ear tags per box cattle and calves.

20 ear tags per box

MERCK ANIMAL HEALTH PROGRAMS

Merck Animal Health is here for you. Your livelihood is our responsibility. You take great care of your animals, so we want to help you. From training modules and industry articles to new technologies and management tips, we have resources for every producer.

Working in collaboration with industry experts, veterinarians and producers, we've developed key programs with information most valuable to our customers. These resources are ever-changing as we continue to work to support the advancement of the dairy and cattle industries.

MERCK ANIMAL HEALTH PROGRAMS

BEEF MARKET CENTRAL®

Proudly brought to you by Merck Animal Health in coordination with DVAuction and *Drovers*, Beef Market Central aims to make every cattle producer's job a little easier by bringing the latest in cattle market information through one real-time dashboard. For more information, visit **BeefMarketCentral.com** or download the app for Apple or Android mobile devices.

DAIRY CARE 365®

For dairy producers, calf ranchers, farm employees, veterinarians and every stakeholder involved in the care and well-being of dairy animals, Dairy Care 365 is a network of support designed to provide relevant resources for empowering a culture of care on dairies. To learn more and implement the program into your operation, visit **DairyCare365.com**.

FECAL EGG COUNT REDUCTION TEST (FECRT)

The Fecal Egg Count Reduction Test (FECRT) is a standardized diagnostic tool to determine if there is potential parasite resistance with your current dewormer. For more information, talk to your Merck Animal Health representative.

PRIMEVAC™

Proper preconditioning improves the efficiency and performance of dairy and beef calves. The first program of its kind to offer optional veterinarian certification (or producer affidavit), PrimeVAC protects from respiratory viruses, clostridial bacteria and internal parasites, giving you a marketing edge and the tools you need to make the most out of your cattle investment. For more information, talk to your Merck Animal Health representative.

RESPONSIBLE BEEF

Merck Animal Health has a deep-seated respect for those they serve in America's cattle industry. Your livelihood is a responsibility we take very seriously, and that responsibility is what drives us to deliver world-class research, product innovations and superior technical service to today's cattle community. Responsible Beef features stories that focus on your community, land, cattle and business. To learn more, visit **ResponsibleBeef.com**.

THE BEST DEFENSE™

As the saying goes, the best defense is a good offense. That´s why using Merck Animal Health vaccines makes such good business sense. Our line of cattle health products gives you the power to get in front of disease before it strikes, tackling it before it gains ground. Instead of treating disease, you can keep producing healthy, profitable cattle. To learn more, visit **The-Best-Defense.com**.

WHISPER® VETERINARY STETHOSCOPE

Many cattle with BRD are misdiagnosed and left untreated, thereby reducing performance in those cattle. Conversely, many calves without BRD are unnecessarily administered an antimicrobial product, increasing treatment costs. The Whisper Veterinary Stethoscope is a simple, noninvasive system used to quickly assess lung health, thereby providing additional information to producers to select an appropriate treatment regimen and provide better care for their animals. To learn more, visit **WhisperCattle.com**.

PERFORMANCE EVALUATION PROGRAM (PEP)

The Performance Evaluation Program (PEP) is a multi-point assessment of proper placement of Revalor and Finaplix implants conducted by the Merck Animal Health technical services team in coordination with sales representatives. To evaluate the placement of the Revalor and Finaplix implants in your feedyard cattle, contact your Merck Animal Health representative.

PRODUCT INFORMATION

Resflor GOLD®
Florfenicol and Flunixin Meglumine

Intervet/Merck Animal Health
PRODUCT INFORMATION
(Florfenicol and Flunixin Meglumine)
Antimicrobial/Non-Steroidal Anti-Inflammatory Drug
NADA 141-299, Approved by FDA.
300 mg/16.5 mg/mL
Sterile

For subcutaneous use in beef and non-lactating dairy cattle only.
Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

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

DESCRIPTION: RESFLOR GOLD® is an injectable solution of the synthetic antibiotic florfenicol and the non-steroidal anti-inflammatory drug (NSAID) flunixin. Each milliliter of sterile RESFLOR GOLD® contains 300 mg florfenicol, 16.5 mg flunixin as flunixin meglumine, 300 mg 2-pyrrolidone, 35 mg malic acid, and triacetin qs.

INDICATION: RESFLOR GOLD® is indicated for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni,* and *Mycoplasma bovis* and control of BRD-associated pyrexia in beef and non-lactating dairy cattle.

DOSAGE AND ADMINISTRATION: RESFLOR GOLD® should be administered once by subcutaneous injection at a dose rate of 40 mg florfenicol/kg body weight and 2.2 mg flunixin/kg body weight (6 mL/100 lb). Do not administer more than 10 mL at each site. The injection should be given only in the neck. Injection sites other than the neck have not been evaluated. For the 500 mL vial, do not puncture the stopper more than 20 times.

RESFLOR GOLD® Dosage Guide*

ANIMAL WEIGHT (lbs)	DOSAGE (mL)
100	6.0
200	12.0
300	18.0
400	24.0
500	30.0
600	36.0
700	42.0
800	48.0
900	54.0
1000	60.0

Recommended Injection Location

*Do not administer more than 10 mL at each site.

CONTRAINDICATIONS: Do not use in animals that have shown hypersensitivity to florfenicol or flunixin.

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains material that can be irritating to skin and eyes. Avoid direct contact with skin, eyes, and clothing. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information.
For customer service or to obtain a copy of the MSDS, call 1-800-211-3573. For technical assistance or to report suspected adverse reactions, call 1-800-219-9286.

PRECAUTIONS: As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Patients at greatest risk for adverse events are those that are dehydrated, on diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully monitored. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that have not been previously diagnosed. Since many NSAIDs possess the potential to produce gastrointestinal ulceration, concomitant use of RESFLOR GOLD® with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided or closely monitored.

Flunixin is a cyclo-oxygenase inhibitory NSAID, and as with others in this class, adverse effects may occur with its use. The most frequently reported adverse effects have been gastrointestinal signs. Events involving suspected renal, hematologic, neurologic, dermatologic, and hepatic effects have also been reported for other drugs in this class.

Not for use in animals intended for breeding purposes. The effects of florfenicol on bovine reproductive performance, pregnancy, and lactation have not been determined. Toxicity studies in dogs, rats, and mice have associated the use of florfenicol with testicular degeneration and atrophy. NSAIDs are known to have potential effects on both parturition and the estrous cycle. There may be a delay in the onset of estrus if flunixin is administered during the prostaglandin phase of the estrous cycle. The effects of flunixin on imminent parturition have not been evaluated in a controlled study. NSAIDs are known to have the potential to delay parturition through a tocolytic effect.

RESFLOR GOLD®, when administered as directed, may induce a transient reaction at the site of injection and underlying tissues that may result in trim loss of edible tissue at slaughter.

RESIDUE WARNINGS: Animals intended for human consumption must not be slaughtered within 38 days of treatment. This product is not approved for use in female dairy cattle 20 months of age or older, including dry dairy cows. Use in these cattle may cause drug residues in milk and/or in calves born to these cows. A withdrawal period has not been established in pre-ruminating calves. Do not use in calves to be processed for veal.

ADVERSE REACTIONS: Transient inappetence, diarrhea, decreased water consumption, and injection site swelling have been associated with the use of florfenicol in cattle. In addition, anaphylaxis and collapse have been reported post-approval with the use of another formulation of florfenicol in cattle. In cattle, rare instances of anaphylactic-like reactions, some of which have been fatal, have been reported, primarily following intravenous use of flunixin meglumine.

CLINICAL PHARMACOLOGY: The pharmacokinetics (PK) of florfenicol (Table 1) and flunixin (Table 2) after subcutaneous injection of RESFLOR GOLD® is described below:

Table 1. Mean (n=28) pharmacokinetic parameters for florfenicol in cattle after a single subcutaneous administration of RESFLOR GOLD® (florfenicol dose of 40 mg/kg BW).

Mean Florfenicol PK parameters in Cattle

PK Parameter	AUC_{0-t}[1] (ng*hr/mL)	$AUC_{0-\infty}$[2] (ng*hr/mL)	C_{max}[3] (ng/mL)	T_{max}[4] (hr)	$T_{1/2}$[5] (hr)	$MRT_{0-\infty}$[6] (hr)
Mean	242527	247077	11161	0.25	23.5	27.3
SD[7]	42741	41381	4154	3.67	9.91	11.6

Table 2. Mean (n=28) pharmacokinetic parameters for flunixin in cattle after a single subcutaneous administration of RESFLOR GOLD® (flunixin dose of 2.2 mg/kg BW).

Mean Flunixin PK parameters in Cattle

PK Parameter	AUC_{0-t}[1] (ng*hr/mL)	$AUC_{0-\infty}$[2] (ng*hr/mL)	C_{max}[3] (ng/mL)	T_{max}[4] (hr)	$T_{1/2}$[5] (hr)	$MRT_{0-\infty}$[6] (hr)
Mean	13235	16442**	1913	1.14	6.37*	11.6
SD[7]	4988	5155	791	0.97	3.37	6.47

[1] AUC_{0-t} = Area under the plasma-concentration-time curve (AUC) from time zero to the last quantifiable concentrations
[2] AUC_{0-inf} = AUC from time zero to infinity
[3] C_{max} = Maximum plasma concentration
[4] T_{max} = Time at which C_{max} was observed
[5] $T^{1/2}$ = Terminal elimination half-life
[6] MRT_{0-inf} = Mean residence time from time zero to infinity
[7] SD = Standard deviation
** n=27

MICROBIOLOGY: Florfenicol is a synthetic, broad-spectrum antibiotic active against many Gram-negative and Gram-positive bacteria isolated from domestic animals. It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis. Florfenicol is generally considered a bacteriostatic drug, but exhibits bactericidal activity against certain bacterial species. *In vitro* studies demonstrate that florfenicol is active against the BRD pathogens *M. haemolytica, P. multocida,* and *H. somni,* and *M. bovis* that florfenicol exhibits bactericidal activity against strains of *M. haemolytica* and *H. somni.*

The minimum inhibitory concentrations (MICs) of florfenicol were determined for non-mycoplasmal BRD isolates obtained from calves enrolled in BRD field studies in the U.S. in 2006 using methods recommended by the Clinical and Laboratory Standards Institute (M31-A2). MICs for *M. bovis* isolates were determined by an accepted method using Hayflick Broth with Alamar Blue (HBAN) medium under appropriate control. Isolates were obtained from pre-treatment nasal swabs from all calves enrolled at all four sites, post-treatment nasal swabs from treatment failures in the RESFLOR GOLD® and saline control treatment groups at three sites, and lung tissue from one calf that died in the saline control treatment group. The results are shown in below Table 3.

Table 3. Florfenicol MIC values* of indicated pathogens isolated from cattle with naturally-occurring BRD

Indicated pathogens	Year of isolation	Number of isolates	MIC_{50}** (µg/mL)	MIC_{90}** (µg/mL)	MIC range (µg/mL)
Mannheimia haemolytica	2006	169	1.0	1.0	0.5 to 32
Pasteurella multocida	2006	139	0.5	0.5	≤ 0.125 to 16
Histophilus somni	2006	84	≤ 0.125	≤ 0.125	≤ 0.125 to 2.25
Mycoplasma bovis	2006	66	1.0	1.0	0.5 to 1.0

* The correlation between *in vitro* susceptibility data and clinical effectiveness is unknown.
** The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

EFFECTIVENESS: In a multi-site field study, calves with naturally-occurring BRD were treated with RESFLOR GOLD®, Nuflor Gold® (NADA 141-265), or saline. A treatment success was defined as a calf with normal respiration to mild respiratory distress, normal attitude to mildly depressed, and a rectal temperature < 104.0 °F on Day 11.

The treatment success rate for BRD for the RESFLOR GOLD® treatment group (68.4%) was statistically significantly greater (p = 0.0255) compared to the saline control treatment group (42.9%). RESFLOR GOLD® was non-inferior to Nuflor Gold® for the treatment of BRD, with a one-sided 95% lower confidence bound for the difference between the two treatments equal to -13.2%.

In the same study, the change in rectal temperature from pre-treatment to six hours post-treatment was evaluated to determine the effectiveness of RESFLOR GOLD® for the control of BRD-associated pyrexia. The proportion of calves whose rectal temperatures decreased by ≥ 2.0 °F from pre-treatment to six hours post-treatment was statistically significantly greater (p = 0.0019) in the RESFLOR GOLD® treatment group compared to the saline control treatment group. The mean decrease in rectal temperature from pre-treatment to six hours post-treatment was statistically significantly greater in the RESFLOR GOLD® treatment group compared to the NUFLOR GOLD® and saline control treatment groups (p = 0.0031 and 0.0002, respectively).

The effectiveness of RESFLOR GOLD® for the treatment of BRD associated with *Mycoplasma bovis* was demonstrated by examining the *M. bovis* data from cattle enrolled in the BRD treatment study described above. There were numerically more treatment successes (6 of 8 calves, 75%) than treatment failures (2 of 8 calves, 25%) in RESFLOR GOLD®-treated calves that cultured positive for *M. bovis* pre-treatment.

ANIMAL SAFETY: A target animal safety study was conducted to evaluate the effects of RESFLOR GOLD® when administered to cattle subcutaneously at 1X, 3X, or 5X the labeled dose for three consecutive days (3X the labeled duration). Decreased feed and water consumption, and decreased body weights (secondary to decreased feed consumption) were observed in the 1X, 3X, and 5X groups. Injection site swellings were noted in the 1X, 3X, and 5X groups.

A separate injection site study was conducted in cattle. The study demonstrated that RESFLOR GOLD®, when administered according to the label directions, may induce a transient local reaction in the subcutaneous and underlying muscle tissue.

STORAGE INFORMATION: Do not store above 30°C (86°F). Use within 28 days of first use.

HOW SUPPLIED: RESFLOR GOLD® is available in 100, 250, and 500 mL sterile, multiple-dose, glass vials.

Made in Germany
Intervet Inc., a subsidiary of Merck & Co., Summit, NJ 07901

Rev. 7/12
122996 R3

100mL Multiple-Dose Vial	
250mL Multiple-Dose Vial	120610 R2
500mL Multiple-Dose Vial	124378 R3

CVP No.: 1047298.3

PRODUCT INFORMATION

NADA #141-063, Approved by FDA.

Nuflor® (FLORFENICOL)

Injectable Solution 300 mg/mL

For intramuscular and subcutaneous use in beef and non-lactating dairy cattle only.
dairy cattle 20 months of age or older or in calves to be processed for veal.

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

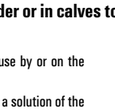
DESCRIPTION NUFLOR Injectable Solution is a solution of the synthetic antibiotic florfenicol. Each milliliter of sterile NUFLOR Injectable Solution contains 300 mg of florfenicol, 250 mg n-methyl-2-pyrrolidone, 150 mg propylene glycol, and polyethylene glycol qs.

INDICATIONS NUFLOR Injectable Solution is indicated for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida,* and *Histophilus somni,* and for the treatment of bovine interdigital phlegmon (foot rot, acute interdigital necrobacillosis, infectious pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*. Also, it is indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica, Pasteurella multocida,* and *Histophilus somni*.

DOSAGE AND ADMINISTRATION For treatment of bovine respiratory disease (BRD) and bovine interdigital phlegmon (foot rot): NUFLOR Injectable Solution should be administered by intramuscular injection to cattle at a dose rate of 20 mg/kg body weight (3 mL/100 lbs). A second dose should be administered 48 hours later. Alternatively, NUFLOR Injectable Solution can be administered by a single subcutaneous (SC) injection to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 lbs). Do not administer more than 10 mL at each site. The injection should be given only in the neck.
NOTE: Intramuscular injection may result in local tissue reaction which persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe.
For control of respiratory disease in cattle at high-risk of developing BRD: Nuflor Injectable Solution should be administered by a single subcutaneous injection to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 lbs). Do not administer more than 10 mL at each site. The injection should be given only in the neck.

NUFLOR Injectable Solution DOSAGE GUIDE		
ANIMAL WEIGHT (lbs)	IM NUFLOR DOSAGE 3.0 mL/100 lb Body Weight (mL)	SC NUFLOR DOSAGE 6.0 mL/100 lb Body Weight (mL)
100	3.0	6.0
200	6.0	12.0
300	9.0	18.0
400	12.0	24.0
500	15.0	30.0
600	18.0	36.0
700	21.0	42.0
800	24.0	48.0
900	27.0	54.0
1000	30.0	60.0

Recommended Injection Location



Do not inject more than 10 mL per injection site.

Clinical improvement should be evident in most treated subjects within 24 hours of initiation of treatment. If a positive response is not noted within 72 hours of initiation of treatment, the diagnosis should be re-evaluated.

CONTRAINDICATIONS Do not use in animals that have shown hypersensitivity to florfenicol.

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains materials that can be irritating to skin and eyes. Avoid direct contact with skin, eyes, and clothing. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information.
For customer service, adverse effects reporting, and/or a copy of the MSDS, call 1-800-211-3573.

PRECAUTIONS: Not for use in animals intended for breeding purposes. The effects of florfenicol on bovine reproductive performance, pregnancy, and lactation have not been determined. Toxicity studies in dogs, rats, and mice have associated the use of florfenicol with testicular degeneration and atrophy. Intramuscular injection may result in local tissue reaction which persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe.

RESIDUE WARNINGS: Animals intended for human consumption must not be slaughtered within 28 days of the last intramuscular treatment. Animals intended for human consumption must not be slaughtered within 38 days of subcutaneous treatment. This product is not approved for use in female dairy cattle 20 months of age or older, including dry dairy cows. Use in these cattle may cause drug residues in milk and/or in calves born to these cows. A withdrawal period has not been established in pre-ruminating calves. Do not use in calves to be processed for veal.

ADVERSE REACTIONS Inappetence, decreased water consumption, or diarrhea may occur transiently following treatment.

CLINICAL PHARMACOLOGY The pharmacokinetic disposition of NUFLOR Injectable Solution was evaluated in feeder calves following single intramuscular (IM) administration at the recommended dose of 20 mg/kg body weight. NUFLOR Injectable Solution was also administered intravenously (IV) to the same cattle in order to calculate the volume of distribution, clearance, and percent bioavailability1 (Table 1).

TABLE 1. Pharmacokinetic Parameter Values for Florfenicol Following IM Administration of 20 mg/kg Body Weight to Feeder Calves (n=10).

Parameter	Median	Range
C_{max} (µg/mL)	3.07*	1.43 - 5.60
t_{max} (hr)	3.33	0.75 - 8.00
$T^{1}/_{2}$ (hr)	18.3**	8.30 - 44.0
AUC (µg•min/mL)	4242	3200 - 6250
Bioavailability (%)	78.5	59.3 - 106
Vd_{ss} (L/kg)***	0.77	0.68 - 0.85
Cl_t (mL/min/kg)***	3.75	3.17 - 4.31

* harmonic mean
** mean value
*** following IV administration

C_{max} Maximum serum concentration
T_{max} Time at which C_{max} is observed
$T^{1}/_{2}$ Biological half-life
AUC Area under the curve
Vd_{ss} Volume of distribution at steady state
Cl_t Total body clearance

Florfenicol was detectable in the serum of most animals through 60 hours after intramuscular administration with a mean concentration of 0.19 µg/mL. The protein binding of florfenicol was 12.7%, 13.2%, and 18.3% at serum concentrations of 0.5, 3.0, and 16.0 µg/mL, respectively.

MICROBIOLOGY Florfenicol is a synthetic, broad-spectrum antibiotic active against many Gram negative and Gram-positive bacteria isolated from domestic animals. It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis. Florfenicol is generally considered a bacteriostatic drug, but exhibits bactericidal activity against certain bacterial species. *In vitro* studies demonstrate that florfenicol is active against the bovine respiratory disease (BRD) pathogens *Mannheimia haemolytica, Pasteurella multocida*, and *Histophilus somni*, and that florfenicol exhibits bactericidal activity against strains of *M. haemolytica and H. somni*. Clinical studies confirm the efficacy of florfenicol against BRD as well as against commonly isolated bacterial pathogens in bovine interdigital phlegmon including *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*.
The minimum inhibitory concentrations (MICs) of florfenicol for BRD organisms were determined using isolates obtained from natural infections from 1990 to 1993. The MICs for interdigital phlegmon organisms were determined using isolates obtained from natural infections from 1973 to 1997 (Table 2).

TABLE 2. Florfenicol Minimum Inhibitory Concentration (MIC) Values* of Indicated Pathogens Isolated From Natural Infections of Cattle.

Indicated pathogens	Year of isolation	Isolate Numbers	MIC_{50}** (µg/mL)	MIC_{90}** (µg/mL)
Mannheimia haemolytica	1990 to 1993	398	0.5	1
Pasteurella multocida	1990 to 1993	350	0.5	0.5
Histophilis somni	1990 to 1993	66	0.25	0.5
Fusobacterium necrophorum	1973 to 1997	33	0.25	0.25
Bacteroides melaninogenicus	1973 to 1997	20	0.25	0.25

* The correlation between the *in vitro* susceptibility data and clinical effectiveness is unknown.
** The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

ANIMAL SAFETY A 10X safety study was conducted in feeder calves. Two intramuscular injections of 200 mg/kg were administered at a 48-hour interval. The calves were monitored for 14 days after the second dose. Marked anorexia, decreased water consumption, decreased body weight, and increased serum enzymes were observed following dose administration. These effects resolved by the end of the study.
A 1X, 3X, and 5X (20, 60, and 100 mg/kg) safety study was conducted in feeder calves for 3X the duration of treatment (6 injections at 48-hour intervals). Slight decrease in feed and water consumption was observed in the 1X dose group. Decreased feed and water consumption, body weight, urine pH, and increased serum enzymes, were observed in the 3X and 5X dose groups. Depression, soft stool consistency, and dehydration were also observed in some animals (most frequently at the 3X and 5X dose levels), primarily near the end of dosing.
A 43-day controlled study was conducted in healthy cattle to evaluate effects of NUFLOR Injectable Solution administered at the recommended dose on feed consumption. Although a transient decrease in feed consumption was observed, NUFLOR Injectable Solution administration had no long-term effect on body weight, rate of gain, or feed consumption.

STORAGE INFORMATION Store between 2°-30°C (36°-86°F). Refrigeration is not required. The solution is light yellow to straw colored. Color does not affect potency.

HOW SUPPLIED NUFLOR Injectable Solution is packaged in 100 mL (NDC 0061-1116-04), 250 mL (NDC 0061-1116-05), and 500 mL (NDC 0061-1116-06) glass sterile multiple-dose vials.

REFERENCE 1. Lobell RD, Varma KJ, et al. Pharmacokinetics of florfenicol following intravenous and intramuscular doses to cattle. J Vet Pharmacol Therap. 1994;17:253-258.

Made in Germany

Rev. 8/12

PRODUCT INFORMATION
NADA #101-479, Approved by FDA.

Banamine®
(FLUNIXIN MEGLUMINE)
Injectable Solution 50 mg/mL Veterinary

Only for Intravenous Use in Beef and Dairy Cattle.
Not for Use in Dry Dairy Cows and Veal Calves.
For Intravenous and Intramuscular Use in Horses.

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

DESCRIPTION Each milliliter of BANAMINE Injectable Solution contains flunixin meglumine equivalent to 50 mg flunixin, 0.1 mg edetate disodium, 2.5 mg sodium formaldehyde sulfoxylate, 4.0 mg diethanolamine, 207.2 mg propylene glycol; 5.0 mg phenol as preservative, hydrochloric acid, water for injection qs.

PHARMACOLOGY Flunixin meglumine is a potent, non-narcotic, nonsteroidal, analgesic agent with anti-inflammatory and antipyretic activity. It is significantly more potent than pentazocine, meperidine, and codeine as an analgesic in the rat yeast paw test.

Horse: Flunixin is four times as potent on a mg-per-mg basis as phenylbutazone as measured by the reduction in lameness and swelling in the horse. Plasma half-life in horse serum is 1.6 hours following a single dose of 1.1 mg/kg. Measurable amounts are detectable in horse plasma at 8 hours postinjection.

Cattle: Flunixin meglumine is a weak acid (pKa=5.82)[1] which exhibits a high degree of plasma protein binding (approximately 99%).[2] However, free (unbound) drug appears to readily partition into body tissues (V_{ss} predictions range from 297 to 782 mL/kg.[2-5] Total body water is approximately equal to 570 mL/kg).[6] In cattle, elimination occurs primarily through biliary excretion.[7] This may, at least in part, explain the presence of multiple peaks in the blood concentration/time profile following IV administration.[2]

In healthy cattle, total body clearance has been reported to range from 90 to 151 mL/kg/hr.[2-5] These studies also report a large discrepancy between the volume of distribution at steady state (V_{ss}) and the volume of distribution associated with the terminal elimination phase (V_β). This discrepancy appears to be attributable to extended drug elimination from a deep compartment.[8] The terminal half-life has been shown to vary from 3.14 to 8.12 hours.[2-5]

Flunixin persists in inflammatory tissues[9] and is associated with anti-inflammatory properties which extend well beyond the period associated with detectable plasma drug concentrations.[4,9] These observations account for the counterclockwise hysteresis associated with flunixin's pharmacokinetic/pharmacodynamic relationships.[10]
Therefore, prediction of drug concentrations based upon the estimated plasma terminal elimination half-life will likely underestimate both the duration of drug action and the concentration of drug remaining at the site of activity.

INDICATIONS *Horse:* BANAMINE Injectable Solution is recommended for the alleviation of inflammation and pain associated with musculoskeletal disorders in the horse. It is also recommended for the alleviation of visceral pain associated with colic in the horse.

Cattle: BANAMINE Injectable Solution is indicated for the control of pyrexia associated with bovine respiratory disease, endotoxemia and acute bovine mastitis. BANAMINE Injectable Solution is also indicated for the control of inflammation in endotoxemia.

DOSE AND ADMINISTRATION *Horse:* The recommended dose for musculoskeletal disorders is 0.5 mg per pound (1 mL/100 lbs) of body weight once daily. Treatment may be given by intravenous or intramuscular injection and repeated for up to 5 days. Studies show onset of activity is within 2 hours. Peak response occurs between 12 and 16 hours and duration of activity is 24-36 hours.

The recommended dose for the alleviation of pain associated with equine colic is 0.5 mg per pound of body weight. Intravenous administration is recommended for prompt relief. Clinical studies show pain is alleviated in less than 15 minutes in many cases. Treatment may be repeated when signs of colic recur. During clinical studies approximately 10% of the horses required one or two additional treatments. The cause of colic should be determined and treated with concomitant therapy.

Cattle: The recommended dose for control of pyrexia associated with bovine respiratory disease and endotoxemia and control of inflammation in endotoxemia, is 1.1 to 2.2 mg/kg (0.5 to 1 mg/lb; 1 to 2 mL per 100 lbs) of body weight given by slow intravenous administration either once a day as a single dose or divided into two doses administered at 12-hour intervals for up to 3 days. The total daily dose should not exceed 2.2 mg/kg (1.0 mg/lb) of body weight. Avoid rapid intravenous administration of the drug.

The recommended dose for acute bovine mastitis is 2.2 mg/kg (1 mg/lb; 2 ml per 100 lbs) of body weight given once by intravenous administration.

CONTRAINDICATIONS *Horse:* There are no known contraindications to this drug when used as directed. Intra-arterial injection should be avoided. Horses inadvertently injected intra-arterially can show adverse reactions. Signs can be ataxia, incoordination, hyperventilation, hysteria, and muscle weakness. Signs are transient and disappear without antidotal medication within a few minutes. Do not use in horses showing hypersensitivity to flunixin meglumine.

Cattle: NSAIDs inhibit production of prostaglandins which are important in signaling the initiation of parturition. The use of flunixin can delay parturition and prolong labor which may increase the risk of stillbirth. Do not use BANAMINE Injectable Solution within 48 hours of expected parturition. Do not use in animals showing hypersensitivity to flunixin meglumine. Use judiciously when renal impairment or gastric ulceration are suspected.

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Milk that has been taken during treatment and for 36 hours after the last treatment must not be used for food. Not for use in dry dairy cows. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. Not for use in horses intended for food. Approved only for intravenous administration in cattle. Intramuscular administration has resulted in violative residues in the edible tissues of cattle sent to slaughter.

PRECAUTIONS As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal and renal toxicity. Sensitivity to drug-associated adverse effects varies with the individual patient. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction.

Since many NSAIDs possess the potential to induce gastrointestinal ulceration, concomitant use of BANAMINE Injectable Solution with other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided or closely monitored.

Horse: The effect of BANAMINE Injectable Solution on pregnancy has not been determined. Studies to determine activity of BANAMINE Injectable Solution when administered concomitantly with other drugs have not been conducted. Drug compatibility should be monitored closely in patients requiring adjunctive therapy.

Cattle: Do not use in bulls intended for breeding, as reproductive effects of Banamine Injectable Solution in these classes of cattle have not been investigated. NSAIDs are known to have potential effects on both parturition (See Contraindications) and the estrous cycle. There may be a delay in the onset of estrus if flunixin is administered during the prostaglandin phase of the estrous cycle. NSAIDs are known to have the potential to delay parturition through a tocolytic effect. The use of NSAIDs in the immediate post-partum period may interfere with uterine involution and expulsion of fetal membranes. Cows should be monitored carefully for placental retention and metritis if Banamine Injectable Solution is used within 24 hours after parturition.

SAFETY *Horse:* A 3-fold intramuscular dose of 1.5 mg/lb of body weight daily for 10 consecutive days was safe.
No changes were observed in hematology, serum chemistry, or urinalysis values. Intravenous dosages of 0.5 mg/lb daily for 15 days; 1.5 mg/lb daily for 10 days; and 2.5 mg/lb daily for 5 days produced no changes in blood or urine parameters. No injection site irritation was observed following intramuscular injection of the 0.5 mg/lb recommended dose. Some irritation was observed following a 3-fold dose administered intramuscularly.

Cattle: No flunixin-related changes (adverse reactions) were noted in cattle administered a 1X (2.2 mg/kg; 1.0 mg/lb) dose for 9 days (three times the maximum clinical duration). Minimal toxicity manifested itself at moderately elevated doses (3X and 5X) when flunixin was administered daily for 9 days, with occasional findings of blood in the feces and/or urine. Discontinue use if hematuria or fecal blood are observed.

ADVERSE REACTIONS In horses, isolated reports of local reactions following intramuscular injection, particularly in the neck, have been received. These include localized swelling, sweating, induration, and stiffness. In rare instances in horses, fatal or nonfatal clostridial infections or other infections have been reported in association with intramuscular use of BANAMINE Injectable Solution. In horses and cattle, rare instances of anaphylactic-like reactions, some of which have been fatal, have been reported, primarily following intravenous use.

HOW SUPPLIED BANAMINE Injectable Solution, 50 mg/ mL, is available in 100-mL (NDC 0061-0851-03), and 250-mL (NDC 0061-0851-04) multi-dose vials.

Store between 2° and 30°C (36° and 86°F).

REFERENCES

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2. Odensvik K, Johansson M. High-performance liquid chromatography method for determination of flunixin in bovine plasma and pharmacokinetics after single and repeated doses of the drug. *Am J Vet Res.* 1995; 56:489-495.
3. Anderson KL, Neff-Davis CA, Davis LE, Bass VD. Pharmacokinetics of flunixin meglumine in lactating cattle after single and multiple intramuscular and intravenous administrations. *Am J Vet Res.* 1990;51:1464-1467.
4. Odensvik K. Pharmacokinetics of flunixin and its effect on prostaglandin $F_{2\alpha}$ metabolite concentrations after oral and intravenous administration in heifers. *J Vet Pharmacol Ther.* 1995;18:254-259.
5. Hardee GE, Smith JA, Harris SJ. Pharmacokinetics of flunixin meglumine in the cow. *Res Vet Sci.* 1985;39:110-112.
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7. Kopcha M, Ahl AS. Experimental uses of flunixin meglumine and phenylbutazone in food-producing animals. *J Am Vet Med Assoc.* 1989;194:45-49.
8. Wagner JG. Significance of ratios of different volumes of distribution in pharmacokinetics. *Biopharm & Drug Dispos.* 1983;4:263-270.
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10. Landoni MF, Cunningham FM, Lees P. Determination of pharmacokinetics and pharmacodynamics of flunixin in calves by use of pharmacokinetic/pharmacodynamic modeling. *Am J Vet Res.* 1995;56:786-794.

April 2012

Made in Germany

MERCK Animal Health

124589 R3

PRODUCT INFORMATION
NADA #141-450, Approved by FDA

Banamine®
Transdermal
(flunixin transdermal solution)

Pour-On for Beef and Dairy Cattle 50 mg/mL

BRIEF SUMMARY: (For full prescribing information, see package insert)

Non-Steroidal Anti-inflammatory Drug

Only for topical use in beef and dairy cattle. Not for use in beef bulls intended for breeding; dairy bulls; female dairy cattle 20 months of age or older, including dry dairy cows; and suckling beef calves, dairy calves, and veal calves.

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

DESCRIPTION: Each milliliter of Banamine Transdermal pour-on contains 50 mg flunixin (equivalent to 83 mg flunixin meglumine), 150 mg pyrrolidone, 50 mg L-menthol, 500 mg propylene glycol dicaprylate/dicaprate NF, 0.20 mg FD&C Red No. 40, and glycerol monocaprylate NF qs.

INDICATIONS: Banamine Transdermal pour-on is indicated for the control of pyrexia associated with bovine respiratory disease and the control of pain associated with foot rot in steers, beef heifers, beef cows, beef bulls intended for slaughter, and replacement dairy heifers under 20 months of age.

CONTRAINDICATIONS: NSAIDs inhibit production of prostaglandins which are important in signaling the initiation of parturition. The use of flunixin can delay parturition and prolong labor which may increase the risk of stillbirth. Do not use Banamine Transdermal pour-on within 48 hours of expected parturition. Do not use in animals showing hypersensitivity to flunixin meglumine.

USER SAFETY WARNINGS: Not for use in humans. Keep out of reach of children. Flunixin transdermal solution is a potent non-steroidal anti-inflammatory drug (NSAID), and ingestion may cause gastrointestinal irritation and bleeding, kidney, and central nervous system effects.

This product has been shown to cause severe and potentially irreversible eye damage (conjunctivitis, iritis, and corneal opacity) and irritation to skin in laboratory animals. Users should wear suitable eye protection (face shields, safety glasses, or goggles) to prevent eye contact; and chemical-resistant gloves and appropriate clothing (such as long-sleeve shirt and pants) to prevent skin contact and/or drug absorption. Wash hands after use.

In case of accidental eye contact, flush eyes immediately with water and seek medical attention. If wearing contact lenses, flush eyes immediately with water before removing lenses. **In case of accidental skin contact and/or clothing contamination, wash skin thoroughly with soap and water** and launder clothing with detergent. **In case of ingestion do not induce vomiting and seek medical attention immediately.** Probable mucosal damage may contraindicate the use of gastric lavage. Provide product label and/or package insert to medical personnel.

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 8 days of the last treatment. Not for use in female dairy cattle 20 months of age or older, including dry dairy cows; use in these cattle may cause drug residues in milk and/or in calves born to these cows or heifers. Not for use in suckling beef calves, dairy calves, and veal calves. A withdrawal period has not been established for this product in pre-ruminating calves.

PRECAUTIONS: As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Patients at greatest risk for adverse events are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction. Banamine transdermal should be used with caution in animals with suspected pre-existing gastric erosions or ulcerations. Concurrent administration of other NSAIDs, corticosteroids, or potentially nephrotoxic drugs should be avoided or used only with careful monitoring because of the potential increase of adverse events.

NSAIDs are known to have potential effects on both parturition (see Contraindications) and the estrous cycle. There may be a delay in the onset of estrus if flunixin is administered during the prostaglandin phase of the estrous cycle. NSAIDs are known to have the potential to delay parturition through a tocolytic effect. The use of NSAIDs in the immediate post-partum period may interfere with uterine involution and expulsion of fetal membranes. Cows should be monitored carefully for placental retention and metritis if Banamine Transdermal pour-on is used within 24 hours after parturition.

Not for use in dairy or beef bulls intended for breeding because reproductive safety has not been evaluated.

HOW SUPPLIED: Banamine Transdermal pour-on, is available in 100-mL (NDC 0061-4363-01), 250-mL (NDC 0061-4363-02), and 1-L (NDC 0061-4363-03) bottles.

Made in Germany
5/2017

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BV-BTD-0001 01/18

F-27865909

Orbenin-DC®
(benzathine cloxacillin)
DRY COW (VACA SECA)

Intramammary Infusion (Infusión intramamaria)

LONG ACTING FORMULA (FÓRMULA DE LARGA ACCIÓN)

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

DESCRIPTION: Orbenin-DC (benzathine cloxacillin) is a stable, nonirritating suspension of benzathine cloxacillin containing the equivalent of 500 mg of cloxacillin per disposable syringe. Orbenin-DC is manufactured by a nonsterilizing process.

Benzathine cloxacillin is a semisynthetic penicillin derived from the penicillin nucleus, 6-amino-penicillanic acid. Benzathine cloxacillin is the benzathine salt of 6-[3-(2-chlorophenyl)-5-methylisoxazolyl-4-carboxamido] penicillanic acid.

The low solubility of Orbenin-DC results in an extended period of activity. Therefore, directions for use should be followed explicitly.

ACTION: Benzathine cloxacillin is bactericidal in action against susceptible organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide. It is active against gram-positive organisms associated with mastitis such as *Staphylococcus aureus* and *Streptococcus agalactiae* and, because of its resistance to penicillinase, penicillin G-resistant staphylococci which may be the cause of mastitis.

Appropriate laboratory tests should be conducted, including *in vitro* culturing and susceptibility tests on pretreatment milk samples collected aseptically.

SUSCEPTIBILITY TEST: The Kirby-Bauer* procedure, utilizing antibiotic susceptibility disks, is a quantitative method that may be adapted to determining the sensitivity of bacteria in milk to Orbenin-DC.

For testing the effectiveness of Orbenin-DC in milk, follow the Kirby-Bauer procedure using the 1 mcg **oxacillin** susceptibility disk. Zone diameters for interpreting susceptibility are:

Resistant	Intermediate	Susceptible
≤ 10 mm	11–12 mm	≥ 13 mm

* Bauer AW, Kirby WMM, Sherris JC, *et al*: Antibiotic testing by a standardized single disk method, *Am J Clin Path* 45:493, 1966. Standardized Disk Susceptibility Test, Federal Register 37:20527–29, 1972.

MERCK Animal Health

INDICATIONS: Orbenin-DC is indicated in the treatment and prophylaxis of bovine mastitis in nonlactating cows due to *Staphylococcus aureus* and *Streptococcus agalactiae.*

CONTRAINDICATIONS: Because benzathine cloxacillin is relatively insoluble, Orbenin-DC's activity will be prolonged. Therefore, Orbenin-DC should not be used for the occasional cow which may have a dry period of less than 4 weeks. This precaution will avoid residues in the milk following removal of the colostrum.

WARNINGS: For use in dry cows only. Do not use within 4 weeks (28 days) of calving. Treated animals must not be slaughtered for food purposes within 4 weeks (28 days) of treatment.

PRECAUTION: Because it is a derivative of 6-amino-penicillanic acid, Orbenin-DC has the potential for producing allergic reactions. Such reactions are rare; however, should they occur, the subject should be treated with the usual agents (antihistamines, pressor amines).

DOSAGE AND ADMINISTRATION: At the last milking of lactation, milk the cow out normally. Clean and disinfect the teats with alcohol swabs provided in the carton, and infuse 1 syringe of Orbenin-DC, which has been warmed to room temperature, into each quarter. Do not milk out. The cow may be milked as usual when she calves.

The extent of subclinical and latent mastitis in a herd is frequently greater than suspected. In untreated herds a significant buildup of subclinical mastitis may occur during the dry period, which results in clinical severity after a few lactations. The adverse influence of subclinical mastitis on milk yield, the risk of cross-infection, and the chance of clinical mastitis flare-up make it necessary to treat the matter as a herd problem. Clinical studies have proven the value of treating all the cows in heavily infected herds as they are dried off. When the herd infection has been reduced, it may be desirable to be more selective in treating infected quarters.

Each carton contains 12 alcohol swabs to facilitate proper cleaning and disinfecting of the teat orifice.

HOW SUPPLIED: Orbenin-DC is supplied in cartons of 12 single-dose syringes with 12 alcohol swabs. Each disposable syringe contains 500 mg of cloxacillin as the benzathine salt in 7.5 g of suitable base.

Do Not Store Above 24°C (75°F)

Orbenin-DC® is a trademark owned by and used under license from SmithKline Beecham.

NADA #55-069, Approved by FDA

Manufactured by:
G.C. Hanford Mfg. Co.
Syracuse, NY 13201

TAKE TIME
OBSERVE LABEL DIRECTIONS

INS15480 03

F-27864503

Amoxi-Mast®
(amoxicillin)

LACTATING COW FORMULA (FÓRMULA PARA VACAS LACTANTES)

Intramammary Infusion (Infusión intramamaria)

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

Amoxi-Mast (amoxicillin) is specially prepared for the treatment of bovine mastitis in lactating cows.

DESCRIPTION: Amoxi-Mast is a stable, nonirritating suspension of amoxicillin trihydrate containing the equivalent of 62.5 mg of amoxicillin per disposable syringe. Amoxi-Mast is manufactured by a nonsterilizing process.

Amoxicillin trihydrate is a semisynthetic penicillin derived from the penicillin nucleus, 6-amino-penicillanic acid. Chemically, it is D(-)-α-amino-p-hydroxybenzyl penicillin trihydrate.

ACTION: Amoxicillin is bactericidal in action against susceptible organisms. It is a broad-spectrum antibiotic which is effective against common infectious mastitis pathogens, namely *Streptococcus agalactiae* and penicillin-sensitive *Staphylococcus aureus.*

In vitro studies have demonstrated the susceptibility of the following strains of bacteria: α- and β-haemolytic streptococci, nonpenicillinase-producing staphylococci, and *Escherichia coli.* Susceptibility has not been demonstrated against penicillinase-producing bacteria, particularly resistant staphylococci. Most strains of Pseudomonas, Klebsiella, and Enterobacter are resistant. The clinical or subclinical significance of these *in vitro* studies is not known.

INDICATIONS: Amoxi-Mast is indicated in the treatment of subclinical infectious bovine mastitis in lactating cows due to *Streptococcus agalactiae* and penicillin-sensitive *Staphylococcus aureus.* Early detection and treatment of mastitis is advised.

MERCK Animal Health

WARNINGS: Milk taken from animals during treatment and for 60 hours (5 milkings) after the last treatment must not be used for food. Treated animals must not be slaughtered for food purposes within 12 days after the last treatment.

PRECAUTION: Because it is a derivative of 6-amino-penicillanic acid, Amoxi-Mast has the potential for producing allergic reactions. Such reactions are rare; however, should they occur, the subject should be treated with the usual agents (antihistamines, pressor amines).

DOSAGE AND ADMINISTRATION: Milk out udder completely. Wash udder and teats thoroughly with warm water containing a suitable dairy antiseptic. Dry thoroughly. Clean and disinfect the teat with alcohol swabs provided in the carton. Remove the syringe tip cover and insert the tip of the syringe into the teat orifice. Express the suspension into the quarter with gentle and continuous pressure. Withdraw the syringe and grasp the end of the teat firmly. Massage the medication up into the milk cistern.

For optimum response, the drug should be administered by intramammary infusion in each infected quarter as described above. Treatment should be repeated at 12-hour intervals for a total of 3 doses. At the next routine milking after the last dose, the treated quarter should be milked out and the milk discarded.

Each carton contains 12 alcohol swabs to facilitate proper cleaning and disinfecting of the teat orifice.

HOW SUPPLIED: Amoxi-Mast is supplied in cartons of 12 single-dose syringes with 12 alcohol swabs. Each 10-mL, disposable syringe contains amoxicillin trihydrate equivalent to 62.5 mg of amoxicillin activity.

Do Not Store Above 24°C (75°F)

TAKE TIME
OBSERVE LABEL DIRECTIONS

NADA #55-100, Approved by FDA

Manufactured by:
G.C. Hanford Mfg. Co.
Syracuse, NY 13201

INS15427 02

F-27865500

Dariclox®
(sodium cloxacillin)

LACTATING COW FORMULA (FÓRMULA PARA VACAS LACTANTES)

Intramammary Infusion (Infusión intramamaria)

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

DESCRIPTION: Dariclox (sodium cloxacillin) is a stable, nonirritating suspension of sodium cloxacillin containing the equivalent of 200 mg of cloxacillin in saturated vegetable oils per disposable syringe. Dariclox is manufactured by a nonsterilizing process.

Cloxacillin is a semisynthetic penicillin derived from the penicillin nucleus, 6-amino-penicillanic acid. Sodium cloxacillin is the monohydrate sodium salt of 5-methyl-3-(o-chlorophenyl)-4-isoxazolyl penicillin.

ACTION: Sodium cloxacillin is bactericidal in action against susceptible organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide. It is active against most gram-positive organisms associated with mastitis. It is effective against *Streptococcus agalactiae* and nonpenicillinase-producing *Staphylococcus aureus*, and there is laboratory evidence that indicates cloxacillin is resistant to destruction by penicillinase-producing organisms. Milk cultures and antibiotic susceptibility testing is recommended when using this product.

SUSCEPTIBILITY TEST: The Kirby-Bauer* procedure, utilizing antibiotic susceptibility disks, is a quantitative method that may be adapted to determining the sensitivity of bacteria in milk to Dariclox.

For testing the effectiveness of Dariclox in milk, follow the Kirby-Bauer procedure using the 1 mcg oxacillin susceptibility disk. Zone diameters for interpreting susceptibility are:

Resistant	Intermediate	Susceptible
≤ 10 mm	11–12 mm	≥ 13 mm

* Bauer AW, Kirby WMM, Sherris JC, *et al.* Antibiotic testing by a standardized single disk method, *Am J Clin Path* 45:493, 1966. Standardized Disk Susceptibility Test, Federal Register 37:20527–29, 1972.

MERCK Animal Health

INDICATIONS: Dariclox is indicated in the treatment of bovine mastitis in lactating cows due to *Streptococcus agalactiae* and nonpenicillinase-producing *Staphylococcus aureus*.

Clinical experience indicates that antibiotic efficacy in the treatment of mastitis in lactating cows is directly related to the duration of infection. Therefore, treatment should be instituted as early as possible after detection.

WARNINGS: Milk taken from animals during treatment and for 48 hours (4 milkings) after the last treatment must not be used for food. Treated animals must not be slaughtered for food purposes within 10 days after the last treatment.

PRECAUTION: Because it is a derivative of 6-amino-penicillanic acid, Dariclox has the potential for producing allergic reactions. Such reactions are rare; however, should they occur, the subject should be treated with the usual agents (antihistamines, pressor amines).

DOSAGE AND ADMINISTRATION: Milk out udder completely. Wash udder and teats thoroughly with warm water containing a suitable dairy antiseptic. Dry thoroughly. Clean and disinfect the teat with alcohol swabs provided in the carton. Remove the syringe tip cover and insert the tip of the syringe into the teat orifice. Express the suspension into the quarter with gentle and continuous pressure. Withdraw the syringe and grasp the end of the teat firmly. Massage the medication up into the milk cistern.

For optimum response the drug should be administered by intramammary infusion in each infected quarter as described above. Treatment should be repeated at 12-hour intervals for a total of 3 doses. The treated quarter should be milked out at the next routine milking.

Each carton contains 12 alcohol swabs to facilitate proper cleaning and disinfecting of the teat orifice.

HOW SUPPLIED: Dariclox is supplied in cartons of 12 single-dose syringes with 12 alcohol swabs. Each 10-mL, disposable syringe contains sodium cloxacillin equivalent to 200 mg of cloxacillin.

Do Not Store Above 24°C (75°F)

TAKE TIME
OBSERVE LABEL DIRECTIONS

NADA #55-070, Approved by FDA

Manufactured by:
G.C. Hanford Mfg. Co.
Syracuse, NY 13201

IN-15476 02

FERTAGYL®
(GONADORELIN)

43 mcg/mL gonadorelin Sterile Solution
FOR THE TREATMENT OF CYSTIC OVARIES IN DAIRY CATTLE
FOR USE WITH ESTRUMATE (CLOPROSTENOL INJECTION) TO SYNCHRONIZE ESTROUS CYCLES TO ALLOW FOR FIXED TIME ARTIFICIAL INSEMINATION (FTAI) IN LACTATING DAIRY COWS

CAUTION
FEDERAL LAW RESTRICTS THIS DRUG TO USE BY OR ON THE ORDER OF A LICENSED VETERINARIAN.

DESCRIPTION
Fertagyl is a sterile solution containing 43 mcg 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
with a molecular weight of 1182.32 and empirical formula $C_{55}H_{72}N_{17}O_{13}$.
Gonadorelin is the hypothalamic releasing factor responsible for the release of gonadotropins (e.g., LH, FSH) from the anterior pituitary.
Synthetic gonadorelin is physiologically and chemically identical to the endogenous bovine hypothalamic releasing factor.

PHARMACOLOGY AND TOXICOLOGY
Endogenous gonadorelin is synthesized by 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 effect the release of gonadotropins (e.g. LH, FSH).
Synthetic gonadorelin administered intramuscularly or intravenously also causes the release of endogenous LH and FSH from the anterior pituitary.
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 untoward effects were noted among rats or dogs administered 120 mcg/kg/day intramuscularly or 72 mcg/kg/day intravenously for 15 days.
It had no adverse effects on heart rate, blood pressure or EKG, when administered to unanesthetized dogs at 60 mcg/kg. In anesthetized dogs it did not produce depression of myocardial or systemic hemodynamics or adversely affect coronary oxygen supply or myocardial oxygen requirements.
The intravenous administration of 60 mcg/kg/day gonadorelin acetate to pregnant rats and rabbits during organogenesis did not cause embryotoxic or teratogenic effects.
The intramuscular administration of 1000 mcg gonadorelin acetate to normally cycling dairy cattle had no effect on hematology or blood chemistry.
Further, gonadorelin acetate did not cause irritation at the site of intramuscular administration in dogs. The dosage administered was 72 mcg/kg/day for 7 days.

INDICATION AND DOSAGE
Cystic Ovaries
Fertagyl (gonadorelin) 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 luteinizing hormone (LH) such as human chorionic gonadotropin.
Fertagyl initiates release of endogenous LH to cause ovulation and luteinization.
The recommended intramuscular or intravenous dosage of Fertagyl is 86 mcg gonadorelin (2 mL) per cow.

Reproductive Synchrony
Fertagyl (gonadorelin) is indicated for use with Estrumate (cloprostenol injection) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.
The recommended intramuscular dosage of Fertagyl is 86 mcg gonadorelin (2 mL) per cow, used in reproductive synchrony programs similar to the following:
- Administer the first Fertagyl injection (2 mL) on Day 0.
- Administer 2 mL of Estrumate (500 mcg cloprostenol, as cloprostenol sodium) by intramuscular injection 6 to 8 days after the first Fertagyl injection.
- Administer the second Fertagyl injection (2 mL) 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.

TARGET ANIMAL SAFETY
In addition to the target animal safety information presented in the section addressing pharmacology and toxicology, target animal safety of, and injection site reactions to, Fertagyl (gonadorelin) when used with Estrumate (cloprostenol injection) were evaluated during the conduct of the effectiveness field studies. The incidence of health abnormalities was not significantly greater in cows administered Fertagyl than cows administered a placebo injection.

EFFECTIVENESS
The effectiveness of Fertagyl (gonadorelin) for use with Estrumate (cloprostenol injection) to synchronize estrous cycles to allow for FTAI in lactating dairy cows was demonstrated in a field study at six different locations in the U.S. A total of 758 healthy, non-pregnant, primiparous or multiparous lactating dairy cows within 50-120 days postpartum were enrolled in the study. A total of 377 cows were administered Fertagyl (2 mL; 86 mcg gonadorelin as the acetate salt) and 381 cows were administered an equivalent volume of saline as an intramuscular injection twice in the following regimen:
Day 0: 2 mL Fertagyl or saline
Day 7: 2 mL Estrumate (cloprostenol injection)
Day 9: 2 mL Fertagyl or saline

Fixed time AI was performed on Day 10, 16 ± 8 hours after the Day 9 injection. Cows were evaluated for pregnancy on 45 ± 5 days by trans-rectal ultrasound or rectal palpation. Pregnancy rate to FTAI was significantly higher (P=0.0051) in cows treated with Fertagyl (33.4%) than the pregnancy rate to FTAI to cows treated with saline (17.8%).

Each mL of Fertagyl contains:

Gonadorelin (as gonadorelin acetate)	43 mcg
Benzyl Alcohol	9 mg
Sodium Chloride	7.47 mg
Water for Injection, USP	q.s.

pH adjusted with sodium phosphate (monobasic and dibasic).
STORAGE CONDITIONS: Keep refrigerated: 2° - 8°C (36° - 46°F).

MERCK Animal Health

PRECAUTIONS
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.

HOW SUPPLIED
Fertagyl is a sterile solution containing 43 mcg gonadorelin (GnRH; as gonadorelin acetate) per milliliter suitable for intramuscular or intravenous administration according to the indication.
Fertagyl is supplied in multidose vials containing 20 mL of sterile solution.

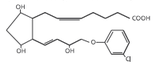
Manufactured for:
Intervet Inc (d/b/a Merck Animal Health)
Madison, NJ 07940
By:
INTERVET INTERNATIONAL GmbH
Unterschleissheim - Germany

141196 R2

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 F2 α (PGF2 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 estrous 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 4 to 5 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 post injection.
   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 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 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.

MERCK Animal Health

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 post treatment. Conception rates may be lower than expected in those fixed time breeding programs 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 Estrumate 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:
Two 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 childbearing 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 bronchiospasms; 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).
4. Use within 28 days of first use.

HOW SUPPLIED:
20-mL multidose vials

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

Made in Germany.

 Code No. 065503 Rev. 5/13

CHORULON®

NADA NO. 140-927; APPROVED BY FDA

FOR ANIMAL USE ONLY

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

DESCRIPTION
CHORULON® is a freeze-dried preparation of chorionic gonadotropin (human Chorionic Gonadotropin or hCG) for intramuscular administration after reconstitution. When reconstituted with the accompanying sterile diluent, each 10 mL vial contains 10,000 I.U. chorionic gonadotropin (equivalent to 10,000 USP Units chorionic gonadotropin) and 10 mg mannitol, with mono- and disodium phosphate to adjust the pH of the solution.

ACTION
Chorionic gonadotropin has luteinizing hormone-like activity with little or no follicle stimulating or estrogenic activity.

INDICATIONS
COWS: CHORULON® is indicated for intramuscular use in cows for the treatment of nymphomania (frequent or constant heat) due to cystic ovaries.
FINFISH: CHORULON® is indicated for use as an aid in improving spawning function in male and female brood finfish.

DOSAGE AND ADMINISTRATION
To reconstitute, transfer the contents of one vial of sterile diluent into one vial of freeze-dried powder. The resulting 10 mL of CHORULON® contains 10,000 I.U. chorionic gonadotropin.
COWS: The contents of one vial (10 mL) of reconstituted CHORULON® should be administered as a single deep intramuscular injection. Dosage may be repeated in 14 days if the animal's behavior or rectal examination of the ovaries indicates the necessity for retreatment.
FINFISH: CHORULON® should be administered via intramuscular injection just ventral to the dorsal fin for one (1) to three (3) injections. Any single injection should be administered, depending on the fish species, at a dose of 50 to 510 I.U./lb body weight (bw) for males and 67 to 1816 I.U./lb bw for females. Depending on body weight and dose administered, it may be necessary to divide the dose among two or more injection sites to avoid injecting a large volume at a single site.
Summaries of doses tested in representative fish species are contained within the following tables. The dose of CHORULON® to be used in other species of finfish may differ from those species listed in the tables, but should fall within the suggested range of 50 to 510 I.U./lb bw for males and 67 to 1816 I.U./lb bw for females.

Table 1: Tested Fish Species/Dose Combinations Found to be Effective

Nomenclature Common Name, *Genus & Species*, Family	Tested Dose(s) [I.U./lb bw/injection] Males	Females	Number of Injections	Injection Interval (h)
yellow perch, *Perca flavescens*, Percidae	nt[1]	67-300	1	-
striped bass, *Morone saxitilis*, Percichthyidae	50-500	75-252	1	-
white bass, *Morone chrysops*, Percichthyidae	65-510	91-750	1	-
razorback sucker, *Xyrauchen texanus*, Catostomidae	nt	100	3	24
walleye, *Stizostedion vitreum*, Percidae	75-400	145-830	1-3	72
red snapper, *Lutjanus campechanus*, Lutjanidae	250	500	1	-
sauger, *Stizostedion canadense*, Percidae	500	500-1000	1	-
Chinese catfish, *Clarius fuscus*, Clariidae	nt	1816	1	-

Footnotes: 1, nt = not tested

Table 2: Tested Fish Species/Dose Combinations Found to be Safe

Nomenclature Common Name, *Genus & Species*, Family	Tested Dose(s) [I.U./lb bw/injection] Males	Females	Number of Injections	Injection Interval (h)
white bass, *Morone chrysops*, Percichthyidae	750	1500	1	-
walleye, *Stizostedion vitreum*, Percidae	750	1500	1	-
grass carp, *Ctenopharyngodon idella*, Cyprinidae	2500	5000	1	-
channel catfish, *Ictalurus punctatus*, Ictaluridae	2500	5000	1	-

ADVERSE REACTIONS
Chorionic gonadotropin is a protein. In the unlikely event of an anaphylactic reaction, epinephrine should be administered. The administration of an antihistamine may also be indicated.

RESIDUE WARNINGS
No withdrawal period is required for cows or brood finfish treated according to label directions. The total dose administered (all injections combined) should not exceed 25,000 I.U. (25 mL) per fish in fish intended for human consumption.

STORAGE AND HANDLING PRECAUTIONS
Store at or below room temperature, 77° F (25°C). Keep out of reach of children. Once reconstituted, CHORULON® should be used immediately. Unused solution should be disposed of properly and not stored for future use.

HOW SUPPLIED
CHORULON® is supplied in cartons containing five vials of freeze-dried powder and five 10 mL vials of sterile diluent. Order Code No. CH-475-1.

Intervet Inc., a subsidiary of Merck & Co. Inc.
Summit, NJ 07901 USA

by:
Intervet International GmbH
Unterschleissheim, Germany

Rev. 4/14

MERCK Animal Health

panacur®
(fenbendazole)
Horse & Cattle **Dewormer**

Shake well before use.
Store at or below 25° C (77° F)
Protect from freezing.

DOSAGE:
Horses: 5 mg/kg (2.3 mg/lb) for the control of large strongyles (*Strongylus edentatus, S. equinus, S. vulgaris, Triodontophorus* spp.), small strongyles (*Cyathostomum* spp., *Cylicocyclus* spp., *Cylicostephanus* spp., *Cylicodontophorus* spp.), and pinworms (*Oxyuris equi*).
EXAMPLE: 2.3 mL/100 lb; 23 mL/1,000 lb

10 mg/kg (4.6 mg/lb) for the control of ascarids (*Parascaris equorum*). EXAMPLE: (10 mg/kg); 2.3 mL/50 lb; 23 mL/500 lb

Beef and Dairy Cattle: 5 mg/kg (2.3 mg/lb) for the removal and control of:

Lungworm (*Dictyocaulus viviparus*).

Stomach worm (adults): *Ostertagia ostertagi* (brown stomach worm). **Stomach worm (adults & 4th stage larvae):** *Haemonchus contortus/placei* (barberpole worm), *Trichostrongylus axei* (small stomach worm).

Intestinal worm (adults & 4th stage larvae): *Bunostomum phlebotomum* (hookworm), *Nematodirus helvetianus* (thread-necked intestinal worm), *Cooperia punctata* and *C. oncophora* (small intestinal worm), *Trichostrongylus colubriformis* (bankrupt worm), *Oesophagostomum radiatum* (nodular worm).

Beef Cattle Only - 10 mg/kg (4.6 mg/lb) for the removal and control of:

Stomach worm (4th stage inhibited larvae): *Ostertagia ostertagi* (Type II Ostertagiasis).

Tapeworm: *Moniezia benedeni*.

▶ Do not use in dairy cattle at 10 mg/kg ◀

In beef and dairy cattle, the recommended dose of 5 mg/kg is achieved when 2.3 mL of the drug are given for each 100 lb of body weight. In beef cattle only, the recommended dosage of 10 mg/kg for the treatment of Ostertagiasis Type II (inhibited 4th stage larvae) or tapeworm is achieved when 4.6 mL of the drug is given for each 100 lb of body weight.

EXAMPLES: (Horses and Cattle)

Dose (5 mg / kg)	Dose (10 mg / kg)	Animal Weight
2.3 mL	4.6 mL	100 lb
4.6 mL	9.2 mL	200 lb
6.9 mL	13.8 mL	300 lb
9.2 mL	18.4 mL	400 lb
11.5 mL	23.0 mL	500 lb
23.0 mL	46.0 mL	1,000 lb
34.5 mL	69.0 mL	1,500 lb

DIRECTIONS:
Beef and Dairy Cattle and Horses: Determine the proper dose according to estimated body weight. Administer orally by suitable dosing syringe. Insert nozzle of syringe through the interdental space and deposit the drug on the back of the tongue by depressing the plunger. The drug may also be administered by stomach tube. There are no known contraindications to the use of the drug in cattle or horses. For dairy cattle, there is no milk withdrawal period at 5 mg/kg. Panacur® (fenbendazole) Suspension 10% is approved for use concomitantly with an approved form of trichlorfon. Trichlorfon is approved for the treatment of stomach bots (*Gasterophilus* spp.) in horses. Refer to the manufacturer's label for directions for use and cautions for trichlorfon.

Regular deworming at intervals of six to eight weeks may be required for horses.

Under conditions of continued exposure to parasites, retreatment of cattle may be needed after 4-6 weeks.

Made in France
Distributed by: **Intervet Inc.**
Madison, NJ 07940
NADA #s 104-494 and 128-620, Approved by FDA

MERCK Animal Health
157767 R1

PRODUCT INFORMATION

141329 R1

BO-SE®
(SELENIUM, VITAMIN E)
Injection

FOR VETERINARY USE ONLY

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

DESCRIPTION BO-SE (selenium, vitamin E) is an emulsion of selenium-tocopherol for the prevention and treatment of white muscle disease (Selenium-Tocopherol Deficiency) syndrome in calves, lambs, and ewes, and as an aid in the prevention and treatment of Selenium-Tocopherol Deficiency in sows and weanling pigs. **Each mL contains:** 2.19 mg sodium selenite (equivalent to 1 mg selenium), 50 mg (68 USP units) vitamin E (as *d*-alpha tocopheryl acetate), 250 mg polysorbate 80, 2% benzyl alcohol (preservative), water for injection q.s. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH.

PHARMACOLOGY It has been demonstrated that selenium and tocopherol exert physiological effects and that these effects are intertwined with sulfur metabolism. Additionally, tocopherol appears to have a significant role in the oxidation process, thus suggesting an interrelationship between selenium and tocopherol in overcoming sulfur-induced depletion and restoring normal metabolism. Although oral ingestion of adequate amounts of selenium and tocopherol would seemingly restore normal metabolism, it is apparent that the presence of sulfur and, perhaps, other factors interfere during the digestive process with proper utilization of selenium and tocopherol. When selenium and tocopherol are injected, they bypass the digestive process and exert their full metabolic effects promptly on cell metabolism. Anti-inflammatory action has been demonstrated by selenium-tocopherol in the Selye Pouch Technique and experimentally induced polyarthritis study in rats.

INDICATIONS BO-SE (selenium, vitamin E) is recommended for the prevention and treatment of white muscle disease (Selenium-Tocopherol Deficiency) syndrome in calves, lambs, and ewes. Clinical signs are: stiffness and lameness, diarrhea and unthriftiness, pulmonary distress and/or cardiac arrest. In sows and weanling pigs, as an aid in the prevention and treatment of diseases associated with Selenium-Tocopherol deficiency, such as hepatic necrosis, mulberry heart disease, and white muscle disease. Where known deficiencies of selenium and/or vitamin E exist, it is advisable, from the prevention and control standpoint, to inject the sow during the last week of pregnancy.

CONTRAINDICATIONS DO NOT USE IN PREGNANT EWES. Deaths and abortions have been reported in pregnant ewes injected with this product.

WARNINGS Anaphylactoid reactions, some of which have been fatal, have been reported in animals administered BO-SE Injection. Signs include excitement, sweating, trembling, ataxia, respiratory distress, and cardiac dysfunction.

Discontinue use 30 days before the treated calves are slaughtered for human consumption. Discontinue use 14 days before the treated lambs, ewes, sows, and pigs are slaughtered for human consumption. Selenium-Vitamin E preparations can be toxic when improperly administered.

PRECAUTIONS Selenium-Tocopherol Deficiency (STD) syndrome produces a variety and complexity of symptoms often interfering with a proper diagnosis. Even in selenium deficient areas there are other disease conditions which produce similar clinical signs. It is imperative that all these conditions be carefully considered prior to treatment of STD syndrome. Serum selenium levels, elevated SGOT, and creatine levels may serve as aids in arriving at a diagnosis of STD, when associated with other indices. Selenium is toxic if administered in excess. A fixed dose schedule is therefore important (read package insert for each selenium-tocopherol product carefully before using).

Important Use only the selenium-tocopherol product recommended for each species. Each formulation is designed for the species indicated to produce the maximum efficacy and safety.

ADVERSE REACTIONS Reactions, including acute respiratory distress, frothing from the nose and mouth, bloating, severe depression, abortions, and deaths have occurred in pregnant ewes. No known treatment exists because at this time the cause of the reaction is unknown.

DOSAGE AND ADMINISTRATION Inject subcutaneously or intramuscularly. Calves: 2.5-3.75 mL per 100 pounds of body weight depending on the severity of the condition and the geographical area. Lambs 2 weeks of age and older: 1 mL per 40 pounds of body weight (minimum, 1 mL). Ewes: 2.5 mL per 100 pounds of body weight. Sows: 1 mL per 40 pounds of body weight. Weanling pigs: 1 mL per 40 pounds of body weight (minimum, 1 mL). Not for use in newborn pigs.

STORAGE **Store between 2° and 30°C (36° and 86°F). Protect from freezing.**

HOW SUPPLIED 100 mL sterile, multiple dose vial, NDC 0061-0807-05.

October 1998

MERCK Animal Health

NADA #30-314, Approved by FDA.

PRODUCT INFORMATION

138188 R1

MU-SE®
(SELENIUM, VITAMIN E)
Injection

FOR VETERINARY USE ONLY

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

DESCRIPTION MU-SE (selenium, vitamin E) is an emulsion of selenium-tocopherol for the prevention and treatment of Selenium-Tocopherol Deficiency (STD) syndrome in weanling calves and breeding beef cattle. **Each mL contains:** 10.95 mg sodium selenite (equivalent to 5 mg selenium), 50 mg (68 USP units) vitamin E (as *d*-alpha tocopheryl acetate), 250 mg polysorbate 80, 2% benzyl alcohol (preservative), water for injection q.s. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH.

ACTIONS It has been demonstrated that selenium and tocopherol exert physiological effects and that these effects are intertwined with sulfur metabolism. Additionally, tocopherol appears to have a significant role in the oxidation process, thus suggesting an interrelationship between selenium and tocopherol in overcoming sulfur-induced depletion and restoring normal metabolism. Although oral ingestion of adequate amounts of selenium and tocopherol would seemingly restore normal metabolism, it is apparent that the presence of sulfur and, perhaps, other factors interfere during the digestive process with proper utilization of selenium and tocopherol. When selenium and tocopherol are injected, they bypass the digestive process and exert their full metabolic effects promptly on cell metabolism. Anti-inflammatory action has been demonstrated by selenium-tocopherol in the Selye Pouch Technique and experimentally induced polyarthritis study in rats.

INDICATIONS MU-SE (selenium, vitamin E) is recommended for the prevention and treatment of STD syndrome in weanling calves and breeding beef cattle. Clinical signs are: stiffness and lameness; chronic, persistent diarrhea; unthriftiness; abortions and/or weak premature calves.

CONTRAINDICATION Do not use in adult dairy cattle. Premature births and abortions have been reported in dairy cattle injected with this product during the third trimester of pregnancy.

WARNINGS **Anaphylactoid reactions, some of which have been fatal, have been reported in cattle administered the MU-SE product. Signs include excitement, sweating, trembling, ataxia, respiratory distress, and cardiac dysfunction.**

Use only as directed in weanling calves and breeding beef cows. Discontinue use 30 days before the treated cattle are slaughtered for human consumption.

DOSAGE AND ADMINISTRATION Inject subcutaneously or intramuscularly. *Weanling calves:* 1 mL per 200 pounds of body weight. *Breeding beef cows:* 1 mL per 200 pounds of body weight during the middle third of pregnancy, and 30 days before calving.

CAUTION Selenium is toxic if administered in excess. A fixed dose schedule is therefore important (read package insert for each selenium-tocopherol product carefully before using).

PRECAUTIONS Selenium-Tocopherol Deficiency (STD) syndrome produces a variety and complexity of symptoms often interfering with a proper diagnosis. Even in selenium deficient areas there are other disease conditions which produce similar clinical signs. It is imperative that all these conditions be carefully considered prior to treatment of STD syndrome. Serum selenium levels, elevated SGOT, and creatine levels may serve as aids in arriving at a diagnosis of STD, when associated with other indices.

Important Use only the selenium-tocopherol product recommended for each species. Each formulation is designed for the species indicated to produce the maximum efficacy and safety.

HOW SUPPLIED 100 mL sterile, multiple dose vial.

STORAGE **Store between 2° and 30°C (36° and 86°F). Protect from freezing.**

MERCK Animal Health

ZUPREVO™ 18%
(Tildipirosin)
Injectable Solution for Cattle

ANTIMICROBIAL DRUG:
180 mg of tildipirosin/mL

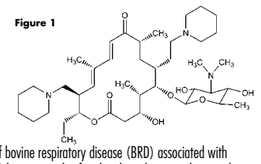
For subcutaneous injection in beef and non-lactating dairy cattle only. Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

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

DESCRIPTION: Zuprevo™ 18% is a ready-to-use sterile injectable solution containing tildipirosin, a semi-synthetic macrolide antibiotic. Each mL of Zuprevo18% contains 180 mg of tildipirosin as the free base, 82.5 mg citric acid monohydrate and 400 mg propylene glycol, and water qs with citric acid monohydrate added to adjust pH.

CHEMICAL NOMENCLATURE AND STRUCTURE:
Tildipirosin is the nonproprietary name for (11E,13E)-(4R,5S,6S,7R,9R,15R,16R)-6-(4-Dimethylamino-3,5-dihydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-16-ethyl-4-hydroxy-5,9,13-trimethyl-7-(2-piperidin-1-yl-ethyl)-15-piperidin-1-ylmethyl-oxacyclohexadeca-11,13-diene-2,10-dione. The empirical formula is $C_{41}H_{71}N_3O_8$. The chemical structure of tildipirosin is shown below.

Figure 1



INDICATIONS: Zuprevo 18% is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida,* and *Histophilus somni* in beef and and non-lactating dairy cattle, and for the control of respiratory disease in beef and non-lactating dairy cattle at high risk of developing BRD associated with *M. haemolytica, P. multocida,* and *H. somni.*

DOSAGE AND ADMINISTRATION: Inject subcutaneously as a single dose in the neck at a dosage of 4 mg/kg (1 mL/100 lb) body weight (BW). Do not inject more than 10 mL per injection site. Do not puncture the stopper of the respective vial size more than the tested number of punctures, shown in Table 1.

Clinical field studies indicate that administration of Zuprevo 18% (tildipirosin) Injectable Solution is effective for the control of respiratory disease in beef and non-lactating dairy cattle at "high risk" of developing BRD. Calves at high risk of developing BRD typically experience one or more of the following risk factors:

- Commingling from multiple sale barns/sources
- Extended transport times and shrink
- Exposure to wet or cold weather conditions or wide temperature swings
- Stressful arrival processing procedures (such as castration, dehorning, or branding)
- Recent weaning and poor vaccination history

Table 1 Number of punctures tested in the in-use study for the respective vial sizes

Vial size [mL]	Number of punctures tested in the in-use study
50	8
100	8
250	16

WARNINGS: FOR USE IN ANIMALS ONLY. NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. TO AVOID ACCIDENTAL INJECTION, DO NOT USE IN AUTOMATICALLY POWERED SYRINGES WHICH HAVE NO ADDITIONAL PROTECTION SYSTEM. IN CASE OF HUMAN INJECTION, SEEK MEDICAL ADVICE IMMEDIATELY AND SHOW THE PACKAGE INSERT OR LABEL TO THE PHYSICIAN.

Avoid direct contact with skin and eyes. If accidental eye exposure occurs, rinse eyes with clean water. If accidental skin exposure occurs, wash the skin immediately with soap and water. Tildipirosin may cause sensitization by skin contact.

For technical assistance or to report a suspected adverse reaction, call: 1-800-219-9286.
For customer service or to request a Material Safety Data Sheet (MSDS), call: 1-800-211-3573.
For additional Zuprevo 18% information go to www.zuprevo.com.
For a complete listing of adverse reactions for Zuprevo 18% reported to CVM see:
http://www.fda.gov/AnimalVeterinary/SafetyHealth.

DO NOT USE ZUPREVO 18% IN SWINE. Fatal adverse events have been reported following the use of tildipirosin in swine. NOT FOR USE IN CHICKENS OR TURKEYS.

RESIDUE WARNING: Cattle intended for human consumption must not be slaughtered within 21 days of the last treatment. Do not use in female dairy cattle 20 months of age or older. Use of this drug product in these cattle may cause milk residues. A withdrawal period has not been established in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS: The effects of Zuprevo 18% on bovine reproductive performance, pregnancy and lactation have not been determined. Swelling and inflammation, which may be severe, may be seen at the injection site after administration. Subcutaneous injection may result in local tissue reactions which persist beyond the slaughter withdrawal period. This may result in trim loss of edible tissue at slaughter.

CLINICAL PHARMACOLOGY: Similar to other macrolides, tildipirosin inhibits essential bacterial protein biosynthesis with selective binding to ribosomal subunits in a bacteriostatic and time-dependent manner. Tildipirosin may be bactericidal against certain isolates of *M. haemolytica* and *P. multocida.*

The following plasma pharmacokinetic (PK) properties of tildipirosin have been observed following a subcutaneous injection at a dose of 4 mg/kg BW in the neck:

Table 2 Summary of pharmacokinetic characterization of tildipirosin administered subcutaneously to calves at a dose of 4 mg/kg BW.

Parameter	Average	SD
C_{max} (ng/mL)	767*	284
T_{max} (hr)	0.75*	0.43
$AUC_{0\text{-}last}$ (hr·ng/mL)	21017**	3499
$AUC_{0\text{-}inf}$ (hr·ng/mL)	24934**	3508
$t_{1/2}$ (hr)	210**	53

* Value based on all 14 animals
** Value based on 8 animals that were slaughtered at 504 hr post-treatment.
C_{max}: maximum observed plasma concentration
T_{max}: Time at which Cmax was observed

$AUC_{0\text{-}last}$: Area under the plasma concentration versus time curve measured from time zero to the last sample with tildipirosin concentrations exceeding the limit of quantification of the analytical method

$AUC_{0\text{-}inf}$: AUC estimated from time zero to time infinity $t_{1/2}$: Terminal elimination half life

Due to the extensive partitioning of macrolides into tissues and because of their multi-fold greater concentrations in bronchial fluid relative to that observed in the blood, plasma drug concentrations underestimate concentrations at the site of action[1]. This is shown for tildipirosin in the following table, where bronchial fluid samples were collected in live, healthy calves, and compared to the concentrations in plasma observed in these same animals:

Table 3 Bronchial fluid-to-plasma ratio of tildipirosin in non-anesthetized cattle following a subcutaneous injection at a dose of 4 mg/kg BW in the neck

Time (hours)	Bronchial fluid (BF) concentration (ng/g)		Plasma (P) concentration (ng/mL)		BF/P Ratio
	Average	SD	Average	SD	
4	1543	895	297	81.8	5.20
10	2975	1279	242	96.7	12.3
24	3448	1433	136	53.9	25.4
72	3489	1712	70.7	29.0	49.3
96	1644	2024	60.2	29.0	27.3
120	1619	1629	52.3	19.9	30.9
240	1937	1416	27.1	10.8	71.5
336	1225	1682	26.1	9.2	47.0
504	935	1032	16.8	1.7	55.6

Tildipirosin concentrations in bronchial fluid collected *in vivo* from non-anesthetized cattle reflect the bacterial exposure to drug concentrations at the site of action.

[1]Nightingale, C.H. (1997) Pharmacokinetics and pharmacodynamics of newer macrolides. The Pediatric Infectious Disease Journal, 16, 438-443.

MICROBIOLOGY: Tildipirosin has shown *in vitro* and *in vivo* antibacterial activity against the bacteria *M. haemolytica, P. multocida,* and *H.somni,* three pathogens associated with BRD.

The minimum inhibitory concentrations (MICs) of tildipirosin against the indicated BRD pathogens were determined using the methods described in the M31-A2 standard of the Clinical and Laboratory Standards Institute (CLSI) and are shown in Table 4.

The MICs of tildipirosin were determined for isolates of *M. haemolytica, P. multocida,* and *H. somni* obtained from two BRD field studies. In both studies, tested isolates of *M. haemolytica* and *P. multocida* were obtained from nasopharyngeal swabs taken prior to treatment from all study animals. Tested isolates of *H. somni* were obtained from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken from saline-treated animals classified as treatment failures.

Table 4 Tildipirosin minimum inhibitory concentration (MIC) values* of indicated pathogens isolated from BRD field studies in the U.S.

Indicated Pathogens	Year of isolation	Study	Number of isolates	MIC50** (µg/mL)	MIC90** (µg/mL)	MIC range (µg/mL)
Mannheimia haemolytica	2007	Treatment	484	1	2	0.25 to >32
	2007 to 2008	Control	178	1	1	0.25 to >32
Pasteurella multocida	2007	Treatment	235	0.5	1	0.12 to >32
	2007 to 2008	Control	273	0.5	1	≤0.03 to 4
Histophilus somni	2007	Treatment	33	2	4	1 to 4
	2007 to 2008	Control	32	2	4	1 to >32

* The correlation between *in vitro* susceptibility data and clinical effectiveness is unknown.
** The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

EFFECTIVENESS: In a multi-location field study, calves with naturally occurring BRD were treated with tildipirosin. The treatment success rate of the tildipirosin-treated group was compared to the treatment success rate in the saline-treated control group. A treatment success was defined as a calf not designated as a treatment failure from Day 1 to 13 and with normal attitude, normal respiration, and a rectal temperature of <104°F on Day 14. The treatment success rate was significantly higher (p=0.003) for the tildipirosin-treated group (229/300, 76%) compared to the saline-treated control group (96/200, 32%). There were no BRD-related deaths in the tildipirosin-treated group compared to a 7% (21/300) BRD-related mortality rate in the saline-treated group.

In another multi-location field study, calves at high risk for developing BRD were administered tildipirosin. The treatment success rate of the tildipirosin-treated group was compared to the treatment success rate in the saline-treated control group. A treatment success was defined as a calf not designated as a treatment failure based on clinical respiratory and attitude scoring and, if necessary, rectal temperature measurement of <104°F through the end of the study (Day 14). The treatment success rate was significantly higher (p=0.0001) for the tildipirosin-treated group (305/386, 79%) compared to the saline-treated group (197/387, 51%). There were three BRD-related deaths during the study (one tildipirosin-treated calf and two saline treated calves).

ANIMAL SAFETY: A target animal safety study was conducted using Zuprevo 18% administered in 5-month-old cattle as three subcutaneous doses of 4, 12, or 20 mg/kg BW given 7 days apart (1X, 3X, and 5X the labeled dose). Animals remained clinically healthy during the study at the labeled dose. Injection site swelling and inflammation, initially severe in some animals, was observed that persisted to the last day of observation (21 days after injection). No other drug-related lesions were observed macroscopically or microscopically at the labeled dose.

A separate injection site tolerance study was conducted using Zuprevo 18% in 5- to 9-month-old cattle administered as a single subcutaneous injection of 10 mL. Injection site swelling and inflammation, initially severe in some animals, was observed that persisted to the last day of observation (35 days after injection). No other drug-related clinical signs were observed.

STORAGE CONDITIONS: Do not store above 30°C (86°F). Do not freeze. The maximum storage time after first puncture is 28 days at or below 25°C (77°F).

HOW SUPPLIED: Zuprevo 18% is supplied in 50, 100 and 250 mL, amber glass, sterile, multi-dose vials.
U. S. Patent: 6,514,946
NADA 141-334, Approved by FDA
Use Only as Directed

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