**INNOVATIVE SOLUTIONS FOR EVERYDAY DAIRY HERD MANAGEMENT** 

# Merck Animal Health Dairy Portfolio





55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 1

ProductPortfolio FA2 ps. 55042 Dairv



9/27/22 7:26 AM

# Merck Animal Health knows dairy.



At Merck Animal Health, we're dedicated to providing a wide range of solutions to meet your dairy's needs. We offer a complete portfolio of trusted products that are backed by science and rooted in innovation. We invest in developing the latest tools, technology and training that accompany our products to help your dairy prosper. We listen to the cows and work with you to provide a holistic approach to animal health. Simply put, we're dairy people. **Merck Animal Health supports you in a way no other company can.** 

55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 1-2

"There are never two days that are the same, and the science and the research that Merck provides helps keep us on the cutting edge. It's innovation and imagination that make us stand above the rest, and Merck is dedicated to helping us do things better. It makes us feel like we've got a true partner." - PAUL WOLCOTT, OWNER, LENT HILL DAIRY, COHOCTON, NEW YORK

# **TABLE OF CONTENTS**

Allflex <sup>®</sup> Livestock Intelligence <sup>®</sup>
Reproduction
Udder Health
Vaccines
BRD Management
Parasite Control
Nutritionals
Dairy Care365°
Product Information

55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 3-4

5
9
13
17
31
37
45
47
49



# MARKET-LEADING MONITORING TECHNOLOGY

Today's dairies are constantly being challenged to do more with less. That's why Allflex Livestock Intelligence works to put the power of information directly into your hands. Allflex provides dairy producers with tools to identify, monitor and trace each individual animal within a herd – making it easier to efficiently manage health, wellbeing and productivity. **Visit AllflexUSA.com** 

"It streamlines treatment, and the cows that really need treatment get it. And the cows that don't? You're not wasting money and labor to do that."

- ANDY BUTTLES, STONE-FRONT FARM, LANCASTER, WISCONSIN





"Since starting Allflex in 2010, we've basically kept the same amount of labor, doubled the herd size and taken our pregnancy rate up 10%."

- SETH ATWATER, ATWATER FARMS, BARKER, NEW YORK

# Animal Monitoring

Allflex's monitoring technology collects and analyzes critical data points for every cow on the dairy – all day, every day. The technology utilizes proprietary algorithms that continually improve to meet the needs of your dairy.<sup>1</sup>



million cows monitored

These systems transform all tracked data into easy-to-read reports that allow you to make critical real-time decisions regarding:

- TRACKING OVERALL HEALTH, HELPS REVEAL NUTRITION with the ability to help identify sick cows one to two days sooner than a physical evaluation.<sup>2</sup>
- HEAT DETECTION AID to improve conception rates while reducing labor and time spent.
- **AND HEAT STRESS** insights within and across specific groups.
- Allowing "cows to be cows" and **REDUCING UNNECESSARY DISRUPTIONS** to their daily routines.



The Allflex Identification portfolio helps streamline breeding, management and milking processes so that your dairy can march ahead with predictable consistency.

As the global leader in animal identification, Allflex provides intelligent solutions for a wide variety of dairy herd needs.

# **VISUAL IDENTIFICATION**

Tags of various sizes and colors can be tailored to the unique ways you manage and market your cattle. Tags are customizable using an ID system with easy-to-read, permanent laser ink.



# **TISSUE SAMPLING UNITS (TSUs)**

Allflex TSUs eliminate the hassle of taking blood or hair samples. One squeeze (similar to a tag application) is all it takes to capture high-quality DNA.



This product is not intended to diagnose, treat, cure, or prevent any disease in animals. For the diagnosis, treatment, cure, or prevention of disease in animals, you should consult your veterinarian. The accuracy of the data collected and presented through this product is not intended to match that of medical devices or scientific measurement devices. 'Stangaferro ML, et al. Use of rumination and activity monitoring for the identification of dairy cows with health disorders: Part I. Metabolic and digestive disorders. J Dairy Sci. 2016;19(9):7395-7410.



55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 7-8

# **ELECTRONIC IDENTIFICATION** (EID)

Based on low-frequency RFID technology, Allflex EID tags are the backbone of digital herd management records. Each tag features a unique 15-digit number for convenient record keeping within your management software.



# ALLFLEX INTELLIGENCE

# **MATCHED SETS**

Matched sets allow you to sync your custom visual tag, EID tag and Tissue Sampling Units (TSUs) together with one identification number for added convenience.



# **RFID READERS**

Allflex offers a variety of handheld readers, such as the AWR300 and LPR for rapid reading of Allflex EIDs.



# OPTIMIZE REPRODUCTIVE EFFICIENCY

Even small improvements in reproduction can have a big impact on a dairy. Fine-tuning your herd's reproduction can lead to greater profitability through increased pregnancy



#### REPRODUCTIVE MANAGEMENT CONSULT

There are many factors that can have an impact on timely and efficient reproduction. We offer thorough guidelines to help you ensure compliance with reproductive protocols, including:

- Product storage and handling
  Synchronization program
  Artificial insemination
- technique

  Monitoring technology
  system integrity

Talk to your Merck Animal Health representative about taking advantage of this service. rates, reduced days open and more heifers entering the milking string earlier.

Talk to your veterinarian about estrus synchronization protocols for your operation.



9/27/22 7:27 AM

# **ESTRUMATE**<sup>®</sup>

(cloprostenol injection)

#### The #1 cloprostenol.<sup>1</sup>

Trusted for more than 40 years, ESTRUMATE is a leading estrus synchronization tool in the dairy space, bringing dairy operations:

- LONG HALF-LIFE of three hours<sup>2</sup>
- EXCELLENT estrous response
- A STRONG LUTEOLYTIC AGENT



**ESTRUMATE IS APPROVED FOR USE** IN DAIRY COWS AND REPLACEMENT **HEIFERS FOR THE FOLLOWING REPRODUCTIVE ISSUES:** 

- Unobserved or nondetected estrus
- Treatment of pyometra or chronic endometritis
- Treatment of mummified fetus
- Treatment of luteal cysts
- Estrus synchronization
- Termination of unwanted pregnancies

Estrumate.com



Allflex

Livestock Intelligence

monitoring technology

generates

reports of cows in heat, helping

you achieve

more timely

breeding

and

higher

conception

rates.

See more

on page 7.

# **FERTAGYL®**

(gonadorelin)

#### The #1 GnRH.<sup>1</sup>

FERTAGYL is approved for use with cloprostenol sodium to synchronize heat cycles and allow for the convenience of fixed-time AI (FTAI) in lactating dairy cows. Using FTAI:

- SUBMITS COWS into Al in a timely manner
- SAVES TIME AND LABOR by increasing reproductive efficiency
- · SIMPLIFIES REPRODUCTIVE MANAGEMENT by facilitating scheduled breeding times



A FEW REASONS WHY FERTAGYL IS THE LEADING GnRH:

- Formulated with gonadorelin acetate for better results<sup>3,4</sup>
- Proven to deliver high ovulation and conception rates<sup>5,6</sup>
- Trusted across the industry for nearly 25 years

Fertagyl.com



"Giving FERTAGYL to our animals - timing the shots and getting cows bred at the optimum time - has made a big difference for us."

- DAVE OECHSNER, OECHSNER DAIRY, BROWNSVILLE, WISCONSIN

# **CHORULON®**

(chorionic gonadotropin)

#### **Reliable treatment for cystic ovaries.**

CHORULON is indicated for treating frequent or constant heat in cows due to cystic ovaries. CHORULON treats cystic ovaries with no required meat or milk withdrawal when used according to label directions.



#### Animalytix MAT January 2021

European Agency for the Evaluation of Medicinal Products, Committee for Veterinary Medicinal Products, Cloprostenol and R-Cloprostenol Summary Report, 1997. Luchterhand M, et al. Merck Animal Health (2018). Fertility response to commercially available GnRH products in lactating cows synchronized with the Double-Ovsynch protocol. "Souza AH, et al. A new presynchronization system (Double-Ovsynch) increases fertility at first postpartum timed AI in lactating dairy cows. *Theriogenology*. 2008;70:208-215. "Luchterhand M, et al. Ovulation and fertility response to commercially available GnRH products in lactating cows synchronized with Double-Ovsynch protocol. Anim Repro Sci. 2019;202:42-48. <sup>6</sup>Souza AH, et al. Comparison of gonadorelin products in lactating dairy cows. *Theriogenology*, 2009;72:271-279.

### product labe

**ESTRUMATE IMPORTANT SAFETY INFORMATION:** Do not administer ESTRUMATE to a pregnant cow unless abortion is desired. Severe localized post-injection clostridial infections have been reported; in rare instances infection has led to death. Women of childbearing age, asthmatics, and persons with respiratory problems should exercise extreme caution when handling ESTRUMATE. ESTRUMATE is readily absorbed through the skin and can cause abortion and/or bronchospasms; direct contact with the skin should be avoided, and accidental spillage on the skin should be washed off immediately with soap and water. For complete safety information, refer to the product label. CHORULON IMPORTANT SAFETY INFORMATION: 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. No withdrawal period is required for cows treated according to label directions. For complete safety information, refer to the product label.

11



FERTAGYL IMPORTANT SAFETY INFORMATION: Not for use in humans. Keep out of reach of children. For complete safety information, refer to the

REPRODUCTION



55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 13-14

# UDDER HEALTH FOR SUPERIOR COWS

Mastitis is an ever-present concern on dairies. It negatively impacts the health of the cow, milk quality and overall profitability. Rely on Merck Animal Health for complete dry cow care, including trusted solutions for mastitis prevention as well as treatment during lactation.

9/27/22 7:27 AM

### **ORBENIN-DC**<sup>™</sup> (benzathine cloxacillin intramammary infusion)

#### Targeted treatment at dry-off.

ORBENIN-DC effectively targets Gram-positive bacteria for producers who want to cure mastitis at dry-off and prevent new infections from taking hold. With zero milk withhold, it also allows fresh cows to move into the milking string faster while reducing antibiotic residue risk.





AVAILABLE IN 144-SYRINGE PAIL OR 12-SYRINGE BOX

#### WHY ORBENIN-DC HAS BEEN TRUSTED FOR MORE THAN FOUR DECADES:

- Targeted treatment of Gram-positive bacteria, the most common cause of subclinical mastitis
- Just as effective as competitor products with a "broad-spectrum" label1
- Zero milk withhold post-calving, after a minimum 28-day dry period following administration at dry-off
- Short tip for partial insertion reduces the risk of new infection

#### OrbeninDC.com

#### ShutOutForDairy.com



"It's not uncommon for a cow to be milking over 100 pounds at dry-off. SHUTOUT gave me reassurance that the teat canal would remain protected."

ALAN OECHSNER, OECHSNER DAIRY, BROWNSVILLE, WISCONSIN

# **SHUTOUT®**

#### A teat sealant designed with your operation in mind.

SHUTOUT provides a physical barrier to prevent environmental bacteria from invading the udder. Using SHUTOUT at dry-off gives producers both an easy and flexible way to prevent new mastitis infections during this critical time.



AVAILABLE IN 144-SYRINGE PAIL OR 24-SYRINGE BOX

#### SHUTOUT INTERNAL TEAT SEALANT:

- Supplements the natural keratin plug in the teat canal • Is highly syringeable for easy administration
- Contains both short- and long-tip options for enhanced flexibility at administration
- Comes with large biodegradable disinfectant wipes

# AMOXI-MAST<sup>®</sup> (amoxicillin

intramammary infusion)

#### The effective, affordable way to cut mastitis losses.

AMOXI-MAST effectively targets Gram-positive bacteria, delivering the lowest cost-per-cure for producers who want to effectively treat clinical mastitis infections and get milk back in the tank fast.



AVAILABLE IN 12-SYRINGE BOX

#### AMOXI-MAST:

- Features a simple, three-treatment regimen over 1.5 days
- Has a short milk withhold of just 60 hours
- $\,\cdot\,$  Delivers a high overall cure rate of  $80\%^{\scriptscriptstyle 6,7}$  or more

#### AmoxiMast.com

Johnson AP, et al. Randomized noninferiority study evaluating the efficacy of 2 commercial dry cow mastitis formulations. J Dairy Sci. 2016;99:593-607. <sup>2</sup>Aruda AG, et al. Randomized noninferiority clinical trial evaluating 3 commercial dry cow mastris preparations, Part 1. *J Dairy Sci*. 2013;96:4419-4435. <sup>3</sup>Aruda AG, et al. Randomized noninferiority clinical trial evaluating 3 commercial dry cow mastris preparations, Part 2. *J Dairy Sci*. 2013;96:439-439-<sup>4</sup>Cox E, et al. Cow-level responses to two commercial dry cow mastris preparations. *J Dairy Sci*. 2013;96:491-4435. <sup>5</sup>Cox Level Performance of ORBENIN-DC vs. SPECTRAMAST DC in Two Commercial Dairies. Merck Animal Health technical bulletin, 2018. Tomazi T, et al. Negatively controlled, randomi 2021;104(3):3364-3385. zed clinical trial comparing different antimicrobial interventions for treatment of clinical mastitis caused by Gram-positive pathogens. J Dairy Sci. Wilson DJ, et al. Comparison of seven antibiotic treatments with no treatment for bacteriological efficacy against bovine mastitis pathogens. J Dairy Sci. 1999;82:1664-1670.

<sup>®</sup>Comparison of endotixin concentrations in BOVILIS<sup>®</sup> J-5 with those in three commercially available Gram-negative, lipopolysaccharide core-antigen vaccines, Merck Animal Health <sup>®</sup>Hogan JS, Smith KL, Todhunter DA, Schoenberger PS. Field trial to determine efficacy of an *E. coli* J5 mastitis vaccine. *J Dairy Sci.* 1992;75:78-84. <sup>®</sup>Field trial to compare the efficacy of BOVILIS<sup>®</sup> J-5 and ENVIRACOR<sup>®</sup> J-5 vaccines against clinical mastitis during early lactation, Merck Animal Health technical bulletin, 2020. nical bulletin 2020 nes Merck Animal Health (

**ORBENIN-DC IMPORTANT SAFETY INFORMATION:** 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 additional information, see the product label. AMOXI-MAST IMPORTANT SAFETY INFORMATION: Milk taken from animals during treatment and for 60 hours (2.5 days) 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 complete information, see the product label

BOVILIS J-5 IMPORTANT SAFETY INFORMATION: This product contains oil adjuvant. In the event of accidental self-injection, seek medical attention immediately. For additional information, see the product label.

15





55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 17-18

# PREVENTION STARTS WITH PROTECTION. PROTECTION STARTS WITH BOVILIS®

The BOVILIS vaccine line from Merck Animal Health is one of the most comprehensive vaccine lines in the industry. It offers a vast number of high-quality solutions that address not only the most common challenges but the most critical.

Industry-leading research is another cornerstone of the BOVILIS portfolio. Over the years, Merck Animal Health has pioneered multiple vaccine innovations, including the use of intranasal technology, as well as a focus on minimizing postvaccination reactions. Because in this industry, it's all about moving your herd forward with as few setbacks as possible.



#### VACCINATION CONSULT

Successful immunization of dairy cattle hinges on doing the little things right, such as:

- Storing at the recommended temperatures
- Proper hygiene during administration
- Accurate dosage and record keeping
- Following modified live vaccine reconstitution steps
- Good colostrum management to ensure calves receive vital antibodies
- Animal husbandry practices that support a herd's overall well-being

Talk to your Merck Animal Health representative to learn more about fine-tuning your vaccination practices for optimum results.

# Clostridial Disease Prevention

Clostridial diseases are caused by bacteria found in soils and the intestinal tract. Clostridia spores are highly resistant and can survive for long periods of time. Disease occurs when they enter the animal and encounter conditions of little or no oxygen, which causes them to multiply and release toxins. Once disease spreads, treatment is usually unsuccessful.

Choosing a proven clostridial vaccine can help prevent potential loss. BOVILIS<sup>®</sup> vaccines offer strong protection against fatal diseases caused by clostridial organisms – and are also proven to result in less post-vaccination stress.<sup>1-3</sup>

Proven Clostridial Vaccines	Clostridium chauvoei	C. haemolyticum	<i>C. novyi</i> , including Type B	<i>C. novyi</i> Type B	<i>C. perfringens</i> Type B	C. perfringens Type C	C. perfringens Type D	C. septicum	C. sordellii	C. tetani	Histophilus somni
BOVILIS° VISION° 7 with SPUR°	•		•			•	•	•	•		
BOVILIS <sup>®</sup> VISION <sup>®</sup> 7 SOMNUS with SPUR <sup>®</sup>	•		•			•	•	•	•		•
$BOVILIS^\circVISION^\circ8withSPUR^\circ$	•	•	•			•	•	•	•		
BOVILIS° VISION° 8 SOMNUS with SPUR°	•	•	•			•	•	•	•		•
$BOVILIS^\circVISION^\circCDwithSPUR^\circ$						•	•				
BOVILIS° VISION° CD-T with SPUR°						•	•			•	
BOVILIS° CAVALRY° 9	•	•		•	•	•	•	•	•	•	
BOVILIS° COVEXIN° 8	•	•		•	•	•	•	•		•	

55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 19-20

19



9/27/22 7:27 AM

# BOVILIS° VISION° 7 with SPUR°

## **BOVILIS° VISION° 7 SOMNUS** with SPUR®

#### The #1 clostridial vaccine for calves.<sup>4</sup> AVAILABLE IN 10-DOSE, 50-DOSE AND 250-DOSE **SHOWN EFFECTIVE AGAINST:** SHOWN EFFECTIVE AGAINST: • C. chauvoei (Blackleg) • C. chauvoei (Blackleg) • *C. novyi* (Black disease) • C. novyi (Black disease) • C. perfringens Types C and D (Enterotoxemia) • *C. perfringens* Types C and D (Enterotoxemia) • *C. septicum* (Malignant edema) • *C. septicum* (Malignant edema) • C. sordellii • H. somni

# **BOVILIS® VISION® CD** with SPUR<sup>®</sup>



SHOWN EFFECTIVE AGAINST: • C. perfringens Types C and D (Enterotoxemia)

Powered-By-Spur.com

**BOVILIS® VISION® CD-T** 

# BOVILIS° VISION° 8 with SPUR°

# **BOVILIS° VISION° 8 SOMNUS** with SPUR®

# AVAILABLE IN 10-DOSE AND 50-DOSE SHOWN EFFECTIVE AGAINST: • C. chauvoei (Blackleg) • *C. haemolyticum* (Bacillary Hemoglubinuria/Red Water)

- C. novyi (Black disease)
- *C. perfringens* Types C and D (Enterotoxemia)
- *C. septicum* (Malignant edema)
- C. sordellii

#### Powered-By-Spur.com

21



AVAILABLE IN 10-DOSE,

50-DOSE AND 250-DOSE

• C. sordellii

Powered-By-Spur.com

AVAILABLE IN 10-DOSE AND 50-DOSE

Powered-By-Spur.com



#### SHOWN EFFECTIVE AGAINST:

- C. chauvoei (Blackleg)
- *C. haemolyticum* (Bacillary Hemoglubinuria/Red Water)
- *C. novyi* (Black disease)
- *C. perfringens* Types C and D (Enterotoxemia)
- *C. septicum* (Malignant edema)
- C. sordellii
- H. somni

#### Powered-By-Spur.com

### AVAILABLE IN 50-DOSE

with SPUR<sup>®</sup>

#### SHOWN EFFECTIVE AGAINST:

- C. perfringens Types C and D
- (Enterotoxemia)
- *C. tetani* (Tetanus)

Powered-By-Spur.com

# **BOVILIS® CAVALRY® 9**

#### AVAILABLE IN 10-DOSE, 50-DOSE AND 125-DOSE

#### SHOWN EFFECTIVE AGAINST:

- C. chauvoei (Blackleg)
- C. haemolyticum (Bacillary Hemoglobinuria/Red Water)
- *C. novyi* Type B
- C. perfringens Type B
- C. perfringens Types C and D (Enterotoxemia)
- C. septicum (Malignant edema)
- C. sordellii
- C. tetani (Tetanus)

ChooseBovilis.com

# **BOVILIS° COVEXIN° 8**





#### SHOWN EFFECTIVE AGAINST:

- C. chauvoei (Blackleg)
- *C. haemolyticum* (Bacillary Hemoglobinuria/Red Water)
- *C. novyi* Type B
- C. perfringens Type B
- C. perfringens Types C and D (Enterotoxemia)
- C. septicum (Malignant edema)
- *C. tetani* (Tetanus)

ChooseBovilis.com







# Reproductive Disease Prevention

In order to maximize reproductive potential, it's important that cows and heifers are protected. Diseases like bovine respiratory disease (BRD) and leptospirosis can lead to significant losses in the form of infertility, abortion and poor milk yield. A strong 23

reproductive management program should focus on the critical breeding and gestation periods – and is certainly not complete without comprehensive fetal protection.

The reproductive vaccine lineup from Merck Animal Health protects cattle against early persistent infection of bovine viral diarrhea (BVD) as well as congenital infection later in pregnancy. Protection begins in the critical first trimester to provide comprehensive fetal protection during all three trimesters.

ChooseBovilis.com



# **BOVILIS° VISTA° 5 L5 SQ CFP**

#### AVAILABLE IN 5-DOSE, 10-DOSE AND 50-DOSE

#### SHOWN EFFECTIVE AGAINST:

- Infectious bovine

# **BOVILIS° VISTA° BVD CFP**



55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 23-24

$PI_3$	BRSV	BVD Type 1, including Type 1b*	BVD Type 2	Leptospira canicola	L. grippotyphosa	L. pomona	L. icterohaemorrhagiae	L. hardjo	L. borgpetersenii serovar Hardjo-bovis <sup>.</sup>	Campylobacter fetus	
•	•	•	•	•	•	•	•	•	•		
•	•	•	•	•	•	•	•	•	•	•	
		•	•								
				•	•	•	•	•			



# **BOVILIS° VISTA° 5 VL5 SQ CFP**

# Respiratory Disease Prevention

BRD has the potential to wreak havoc on dairy farms. Beyond the direct cost of treatment, the BRD complex can lead to reduced growth, added time to first calving, increased calving difficulty and lower milk production. It's the second-leading cause of death in



"The technology behind BOVILIS NASALGEN 3 gives me a lot of confidence. It's an intranasal, so my experience is we get an immunogical response in a less stressful manner." TERA BARNHARDT, DVM, JOHNSON CITY, KANSAS

pre-weaned dairy heifers and the leading cause of death in weaned heifers.<sup>5</sup>

Vaccination is a critical step in reducing the incidence of BRD in your herd. The respiratory vaccine portfolio from Merck Animal Health offers multiple routes of administration, proven efficacy and strong duration of immunity.

ChooseBovilis.com



### Respiratory Vaccine Portfolio IBR BOVILIS° VISTA° ONCE SQ BOVILIS° VISTA° 5 SQ • BOVILIS° VISTA° BVD CFP BOVILIS° ONCE PMH° SQ BOVILIS° ONCE PMH° IN BOVILIS® NASALGEN® 3-PMH • BOVILIS° NASALGEN° 3 • BOVILIS° NASALGEN° IP

# **BOVILIS° VISTA° ONCE SQ**

•



50-DOSE

#### SHOWN EFFECTIVE AGAINST:

- Infectious bovine rhinotracheitis (IBR)
- Parainfluenza-3 (Pl<sub>3</sub>) virus Bovine respiratory syncytial virus (BRSV)
- Bovine viral diarrhea (BVD) Types 1, including Type 1b, and 2
- P. multocida
- M. haemolytica

55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 25-26

25

$PI_3$	BRSV	BVD Type 1, including Type 1b	BVD Type 2	Mannheimia haemolytica	Pasteurella multocida
•	•	•	•	•	•
•	•	•	•		
		•	•		
				•	•
				•	•
•	•			•	•
•	•				
•					

# BOVILIS° VISTA° 5 SQ

# **BOVILIS® VISTA® BVD CFP**





Coronavirus • C. perfringens Types C and D

- (Enterotoxemia)
- *E. coli* Type K99

GuardianForCattle.com

immune response - calves look better, and they do

better. Plus, it makes a little tint on the calf's nose,

so you know they've had their dose."

- J. HALL, HALL'S CALF RANCH, LUXEMBURG, WISCONSIN

iry	Scours Vaccines	Bovine coronavirus	Clostridium perfringens Type C	C. perfringens Type D	Escherichia coli Type K99	Rotavirus Group A Serotype G6	
	BOVILIS° GUARDIAN°	•	•	•	•	•	
	BOVILIS® CORONAVIRUS	•					

VACCINES - SCOURS



# Pinkeye Prevention

Pinkeye has been a long-standing problem for cattle producers, with the potential to leave lasting eye damage and cause performance setbacks. While all animals are susceptible to it, calves tend to experience more severe infections.

Pinkeye is primarily thought to be caused by the bacteria *Moraxella bovis* – but a recent study found up to 80% of cases include Moraxella bovoculi alone or along with *M. bovis.*<sup>6</sup> The pinkeye vaccines from Merck Animal Health work in tandem with other management strategies to help prevent pinkeye in both cows and calves.

StopCattlePinkeye.com

#### Pinkeye **Prevention**

BOVILIS° 20/20 VISION° 7 with SPUR° BOVILIS° PILIGUARD° PINKEYE BOVILIS° PILIGUARD° PINKEYE +7 MORAXELLA BOVOCULI BACTERIN

# BOVILIS° 20/20 VISION° 7 with SPUR

#### AVAILABLE IN 10-DOSE AND 50-DOSE

#### SHOWN EFFECTIVE AGAINST:

- *M. bovis* (Pinkeye or infectious bovine keratoconjunctivitis)
- C. chauvoei (Blackleg)
- *C. septicum* (Malignant edema) • *C. novyi* (Black disease)
- C. sordellii
- C. perfringens Types C and D (Enterotoxemia)

## **BOVILIS° PILIGUARD° PINKEYE +7**

#### AVAILABLE IN 10-DOSE AND 50-DOSE SHOWN EFFECTIVE AGAINST:

- *M. bovis* (Pinkeye or infectious bovine keratoconjunctivitis)
- C. chauvoei (Blackleg)
- *C. septicum* (Malignant edema)
- C. novyi (Black disease)
- C. sordellii
- C. perfringens Type B
- C. perfringens Types C and D (Enterotoxemia)

<sup>1</sup>FTR 92-3 Vision 8 Injection Site Blemish Study <sup>2</sup>FTR 96-2 Analysis of Post-Vaccinal Injection Sites Using Ultrasound.
<sup>3</sup>FTR 96-4 Evaluation of Injection Site Blemishes Using Ultrasonography Following Administration of Two Commercial Multivalent Clostridial Vaccines.
<sup>4</sup>Based on Animalytix data 1/1/2021-12/1/2021.



29



# **BOVILIS° PILIGUARD° PINKEYE**



AVAILABLE IN 10-DOSE AND 50-DOSE

#### SHOWN EFFECTIVE AGAINST:

• *M. bovis* (Pinkeye or infectious bovine keratoconjunctivitis)





## MORAXELLA BOVOCULI BACTERIN

AVAILABLE IN 10-DOSE AND 50-DOSE

#### SHOWN EFFECTIVE AGAINST:

• *M. bovoculi* (Pinkeye or infectious bovine keratoconjunctivitis)



<sup>s</sup>Respiratory Diseases in Dairy Calves. University of Kentucky College of Agriculture, Food and Environment, Department of Animal & Food Sciences. <sup>s</sup>Addison, B. New Findings with Bovine Pinkeye. June 2018. Progressive Dairy. https://www.progressivedairy.com/topics/herd-health/new-findings-with-bovinepinkeye. Accessed Feb 3, 2020.



Even with the best prevention methods in place, bovine respiratory disease (BRD) can sneak into your operation and leave a lasting impact. Merck Animal Health offers a robust portfolio of industry-leading anti-infectives and non-steroidal anti-inflammatory drugs (NSAID) to deliver the right treatment at the right time. Multiple products in the portfolio provide improved, cost-effective outcomes for dairy calves and heifers under 20 months of age.

55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 31-32

# THE RIGHT ANTIBIOTIC SOLUTION FOR THE SITUATION

# **RESFLOR GOLD**<sup>®</sup> (florfenicol and

flunixin meglumine)

# Treat BRD the smart way with the original dual therapy option.

RESFLOR GOLD is the industry-standard dual therapy, combining the powerful antibiotic florfenicol and the trusted NSAID flunixin meglumine. Together, they quickly target the infection of BRD and reduce BRD-associated fever. With RESFLOR GOLD, improvement in fever can be seen in as little as six hours.



- Mycoplasma bovis
- Control of BRD-associated pyrexia

#### ResflorGold.com

### **AROVYN**<sup>™</sup> (tulathromycin injection)

#### Harness the power of tulathromycin.

AROVYN is a cost-effective choice for dairy producers who want to manage BRD with tulathromycin. Producers receive all the benefits of tulathromycin, plus the benefits of working with Merck Animal Health BRD experts.



#### ArovynForBRD.com

AROVYN IMPORTANT SAFETY INFORMATION: AROVYN has a pre-slaughter withdrawal time of 18 days in cattle. Do not use in female dairy cattle 20 months of age or older. Do not use in animals known to be hypersensitive to the product. See full Prescribing Information.

**RESFLOR GOLD IMPORTANT SAFETY INFORMATION:** Not for use in humans. Keep out of reach of children. Do not use in animals that have shown hypersensitivity to florfenicol or flunixin. Avoid direct contact with skin, eyes and clothing as product contains materials that can be irritating. 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. Not for use in animals intended for breeding purposes. See package insert for complete information.

**NUFLOR 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 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 pre- ruminating calves. Do not use in calves to be processed for veal. Not for use in animals intended for breading 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. WITH Do not use in animals that have shown hypersensitivity to florfenicol or animals intended for breeding purposes. Transient inappetence, diarrhea, decreased water consumption, injection site swelling, anaphylaxis and collapse have been associated with the use of florfenicol in cattle. Do not use in nilk and/or in calves bor to these cows. Animals intended for human consumption must not be slaughtered within 28 days of the last intramuscular injections are solved by a fug are solved in returned for human to an any sevent with the use of florfenicol in cattle. Do not use in alime shale bary cause drug residues in milk and/or in calves bor to these cows. Animals intended for human consumption must not be slaughtered within 28 days of the last intramuscular treatment or 38 days of subcutaneous treatment. A withdrawal period has not been established in pre-ruminating calves. Avoid direct contact with skin, eyes, and clothing. Pregnant women should wear gloves and exercise caution or avoid handling this product. For complete information, see the product package insert.

**ZUPREVO 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. 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 residue. 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. 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.

#### 33

# ZUPREVO<sup>®</sup> (tildipirosin)

#### The fast BRD treatment that lasts.

ZUPREVO is rapidly absorbed, long-lasting – and all in one cost-effective low-volume dose.

- ZUPREVO reaches peak plasma levels just 45 minutes after administration<sup>2</sup>
- Lasts 28 days in the lungs against *M. haemolytica* and *P. multocida* and 14 days against *H. somni*\*<sup>2</sup>
- A low-volume dose of 1 mL/100 lbs. means less handling and more doses per bottle



#### Lasts 28 days in the lungs<sup>\*</sup>

#### AVAILABLE IN 50-mL, 100-mL AND 250-mL VIALS

# A DOSE OF 1 ML/100 LBS. MEANS LESS HANDLING AND MORE DOSES PER BOTTLE:

- Mannhaemia haemolytica
- Pasteurella multocida
- Histophilus somni

#### Zuprevo.com

The correlation between pharmacokinetic data and clinical effectiveness is unl



# NUFLOR® (florfenicol)

# A proven BRD treatment for over 25 years.

NUFLOR is a tried and trusted antibiotic for the treatment of BRD, foot rot and control of respiratory disease in cattle at high risk of developing BRD.

- Eliminates 99.9% of BRD-causing bacteria within 24 hours<sup>1</sup>
- Continues eliminating bacteria for 68 hours and remains inhibitory through 96 hours<sup>1</sup>









AVAILABLE IN 100-mL, 250-mL AND 500-mL VIALS

#### INDICATED FOR NON-LACTATING DAIRY CATTLE FOR THE TREATMENT OF BRD AND CONTROL OF RESPIRATORY DISEASE IN ANIMALS AT HIGH RISK OF DEVELOPING BRD ASSOCIATED WITH:

- Mannhaemia haemolytica
- Pasteurella multocida
- Histophilus somni

NUFLOR IS ALSO INDICATED FOR THE TREATMENT OF FOOT ROT ASSOCIATED WITH FUSOBACTERIUM NECROPHORUM AND BACTEROIDES MELANINOGENICUS.

Nuflor.com

iown.



55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 35-36

## **BANAMINE TRANSDERMAL®**

(flunixin transdermal solution)

#### Relief is in the palm of your hand.

BANAMINE TRANSDERMAL is the first FDA-approved pour-on for cattle that can reduce fever caused by BRD and pain due to foot rot. The convenient application mode requires less handling, resulting in less stress on your herd during an already stressful time.



AVAILABLE IN 100-DOSE 250-DOSE AND 1-L DOSE

• Absorbs into the blood stream quickly to control pain and fever

Absorbs quickly into the bloodstream

• BQA-friendly with the gentle application eliminating injection-site lesions

**BANAMINE TRANSDERMAL IS INDICATED FOR THE CONTROL OF PYREXIA** ASSOCIATED WITH BRD AND **THE CONTROL OF PAIN** 

ASSOCIATED WITH FOOT ROT IN REPLACEMENT DAIRY HEIFERS UNDER 20 MONTHS OF AGE.

BanamineTD.com

<sup>1</sup>Varma, KJ, Lockwood PW, Cosgrove MS, Rogers ER, Pharmacology, Safety and Clinical Efficacy of Nuflor (florfenicol) Following Subcutaneous Administration to Cattle. Proceedings of a Symposium Held in Conjunction with the XX World Buiatrics Congress. Sydney, Australia. July 1998:13-19. <sup>2</sup>Menge M, et al. Pharmacokinetics of tildipirosin in bovine plasma, lung tissue, and bronchial fluid (from live, non-anesthetized cattle). J Vet Pharm Ther. 2011;1349:1365-2885.

BANAMINE TRANSDERMAL IMPORTANT SAFETY INFORMATION: KEEP OUT OF REACH OF CHILDREN. Only for topical use in beef and dairy cattle. Do not use Banamine Transdermal pour-on within 48 hours of expected parturition. Do not use in animals showing hypersensitivity to flunixin meglumine. 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. Not for use in dairy or beef bulls intended for breeding because reproductive safety has not been evaluated. BANAMINE IMPORTANT SAFETY INFORMATION: 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 pre-ruminating 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.

• The pour-on application makes it easier to administer – for both you and your cattle

# **BANAMINE**<sup>®</sup>

(flunixin meglumine injection)

#### The cattle industry's pioneer NSAID.

BANAMINE is a long-trusted NSAID that works quickly to control inflammation within two hours of administration.



Begins working in **2 HOURS** 



AVAILABLE IN 25-mL AND 100-mL VIALS **BANAMINE IS INDICATED** FOR THE CONTROL OF **PYREXIA ASSOCIATED** WITH BRD, ENDOTOXEMIA AND ACUTE BOVINE MASTITIS, AND CONTROL OF INFLAMMATION IN ENDOTOXEMIA.

The-BRD-Experts.com



55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 37-38

# PROVEN PARASITE CONTROL IN A VARIETY OF FORMULATIONS

If left unchecked, parasites prey on your herd's productivity and your profitability. Choosing the right dewormer is an important decision that can



help prevent this from happening. That's why Merck Animal Health offers a variety of products in a range of formulations targeting both internal and external parasites to keep your cattle protected and your operation thriving.

# Internal Parasite Control

Internal parasites can quietly impact your herd's performance by reducing dry matter intake, milk production and conception rate. Parasites also directly suppress the immune system, which decreases the animal's ability to fight infection and effectively respond to vaccines.

SAFE-GUARD<sup>®</sup> (fenbendazole) and PANACUR<sup>®</sup> (fenbendazole) take care of the toughest internal parasites, all while providing flexibility you can count on.

SafeGuardWorks.com



#### Internal **Parasite Control**

	SAFE-GUARD <sup>®</sup> Suspension (Drench)
	SAFE-GUARD <sup>®</sup> Paste
	SAFE-GUARD° En-Pro-AL° Molasses Block
	SAFE-GUARD° Protein Block
	SAFE-GUARD <sup>®</sup> Free-Choice Mineral
	SAFE-GUARD <sup>®</sup> Alfalfa-Based Pellets
	PANACUR <sup>®</sup> Suspension (Drench) <sup>*</sup>
D	ANACLIP is only approved for dairy sattle at a 5 mg /kg sate



### **SAFE-GUARD**<sup>®</sup> Suspension (Drench)

Paste



AVAILABLE IN 1L, 10L AND 1GAL

- 1 L deworms 43,478 lbs. of cattle • 10 L deworms 434,780 lbs. of cattle
- 1 gal. deworms 164,565 lbs. ofcattle

39

Bankrupt worm     (adult and L4)	Barberpole worm (adult and L4)	Brown stomach worm     (adult)	Hookworm (adult and L4)	• • Lungworm (adult)	Nodular worm     (adult and L4)	Small stomach worm     (adult and L4)	Small intestinal worm     (adult and L4)	Thread-necked intestinal
	•	•	•	•	•	•	•	•

# **SAFE-GUARD** All these years and still 98.7% effective.

SAFE-GUARD is a member of the benzimidazole class of dewormers and is proven effective in the face of parasite resistance – making it a powerful choice to use as part of a strategic deworming protocol.<sup>2</sup>

# **SAFE-GUARD**°

## **SAFE-GUARD**° **Protein Block**





## SAFE-GUARD° En-Pro-AL° Molasses Block



SAFE-GUARD<sup>®</sup>

32SG Mineral Dewormer



41

9/27/22 7:28 AM

# **External Parasite Control**

External parasites, such as flies, lice and ticks, are more than just a nuisance on a dairy. They disrupt daily patterns that result in reduced milk production and increased risk of infection and disease within the herd. Parasite control in calves is especially important to support healthy growth and productivity. *MAHCattle.com* 

External Parasite Control	Lice	Horn flies	Face flies	Horse flies	Stable flies	Mosquitoes	Black flies	Ticks
ULTRA BOSS <sup>®</sup> Pour-On Insecticide	•	•	•	•	•	•	•	•
ULTRA SABER <sup>™</sup> Pour-On Insecticide	•	•						
SYNERGIZED DELICE <sup>®</sup> Pour-On Insecticide	•	•	•	•	•	•	•	
DOUBLE BARREL® VP Insecticide Ear Tags		•	•					



### ULTRA BOSS<sup>®</sup> Pour-On Insecticide

#### AVAILABLE IN 10T AND 1GAL

- 5% permethrin formulation with 5% piperonyl butoxide optimizes control<sup>3</sup>
- Effective horn fly control for 8 weeks; also controls face flies<sup>3</sup>
- Season-long lice control with one application (January through April)<sup>3</sup>
- No milk discard<sup>4</sup>
- 1 qt. Squeeze 'N' Measure Bottle<sup>™</sup> treats 57 550-lb. cattle
- 1 gal. treats 229 550-lb. cattle

### SYNERGIZED DELICE® Pour-On Insecticide

#### AVAILABLE IN 1GAL

- Ready to use, no mixing required • Migrates over animal's skin and
- hair coat for maximum coverage
- Convenient application methods: pour on animal, spray on animal and spray on premises
- · Oil-based for application that holds up any time of year
- 1 gal. treats 46 550-lb. cattle

#### Data on file. Merck Animal Health

Parasite resistance may develop to any de Chemical Watch Factsheet. Piperonyl Butoxide (PBO). Pesticides and You. Beyond Pesticides/National Coalition Against the Misuse of Pesticides. 2006;20(1):17-20. Dobson R, Jackson R, Levecke B, Besier B, et al. Guidelines for fecal egg count reduction tests (FECRT). World Association for the Advancement of Veterinary Parasitology (WAAVP) (2001) oceedings: 23rd Inte of the World

55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 43-44



### ULTRA SABER<sup>™</sup> Pour-On Insecticide<sup>\*</sup>

AVAILABLE IN 30-OZ AND 1GAL

- · Contains 1% lambda-cyhalothrin insecticide with 5% piperonyl butoxide, a synergist that enhances insecticidal activity<sup>3</sup>
- Provides rapid knockdown of flies and consistently provides significant reduction in fly pressure<sup>3</sup>
- From 87% to 99% reduction in fly pressure for eight weeks<sup>1</sup>
- One 30-oz. Squeeze 'N' Measure Bottle<sup>™</sup> treats 90 550-lb. cattle
- 1 gal. treats 378 550-lb. cattle

\*Ultra Saber is not approved for dry or lactating dairy cows

### DOUBLE BARREL<sup>®</sup> VP **Insecticide Ear Tags**

AVAILABLE IN ONE 20-TAG BOX



- Combines two different active ingredients - an organo-phosphate and a synthetic
- pyrethroid which minimizes resistance development and eliminates the need for ear tag rotation
- Unique triangular shape prevents tag from breaking off at neck
- 20 tags and buttons per box
- One 20-tag box treats 10 head of cattle (use two tags per head)

- IMPORTANT SAFETY INFORMATION FOR SAFE-GUARD Suspension (Drench) and Paste: 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. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.
- IMPORTANT SAFETY INFORMATION FOR SAFE-GUARD En-Pro-AL Molasses Block and Protein Block: Cattle must not be slaughtered within 11 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. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.
- IMPORTANT SAFETY INFORMATION FOR SAFE-GUARD Free-Choice Mineral and Alfalfa-Based Pellets: Cattle must not be slaughtered within 13 days following last treatment. For dairy cattle, there is no milk withdrawal. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.
- **PANACUR IMPORTANT SAFETY INFORMATION:** Cattle must not be slaughtered for human consumption within 8 days following treatment. For dairy cattle, there is no milk withdrawal period at the 5mg/kg dose. Do not use at 10mg/kg in dairy cattle. Dose rate of 10mg/kg is for beef cattle only. Dose rate of 10mg/kg in dairy cattle could result in violative residues in milk. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal. Federal law restricts this drug to use by or on the order of a licensed veterinarian.



# MEET NUTRITIONAL NEEDS FROM THE START

White muscle disease, also known as nutritional myopathy of calves, is associated with selenium and/or vitamin E deficiencies – two critical dietary components for cattle. This is especially devastating to young calves, as affected calves will show signs of weakness, stiffness and a reluctance to stand.

MAHCattle.com

# **BO-SE°** Injection

An emulsion of seleniumtocopherol for the prevention and treatment of white muscle disease (selenium-tocopherol deficiency syndrome) in calves.



AVAILABLE IN 100 ML

# **MU-SE°** Injection

An emulsion of seleniumtocopherol for the prevention and treatment of white muscle disease (selenium-tocopherol deficiency syndrome) in weanling calves.



AVAILABLE IN 100 ML

**BO-SE IMPORTANT SAFETY INFORMATION:** 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. 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.

**MU-SE IMPORTANT SAFETY INFORMATION:** 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.



"DAIRY CARE365 has changed the way I do my job. If I'm having difficulty moving an animal, I'm more likely to stop and reevaluate what I'm doing."

- SARA HANSON DE PERALTA, DVM, MAYVILLE ANIMAL CLINIC, MAYVILLE, WISCONSIN



# EMPOWERING THE BEST CARE EVERY DAY

The support Merck Animal Health provides dairy producers and veterinarians goes far beyond any sales transaction. That's why we're proud to offer value-added training through DAIRY CARE365.

DAIRY CARE365° is designed to complement and help fulfill the animal care guidelines of the National Dairy FARM Program: Farmers Assuring Responsible Management<sup>™</sup>.

It offers e-learning modules (available in English and Spanish), standard operating procedures and other resources to help dairy producers train employees in proper animal care and handling. Launched in 2012, this industry-wide collaboration has reached thousands of employees on dairies across the U.S.



55042\_Dairy\_ProductPortfolio\_FA2\_ps.indd 47-48

# DAIRY CARE 365°

- Available learning modules include: Introduction to Dairy Stockmanship • Moving Cows to the Milking Parlor • Low-Stress Handling of Calves and Heifers • Humane Euthanasia Handling Non-ambulatory Cows Newborn Care and Handling Calf Handling and Stockmanship • Bioawareism #1 - Biosecurity
- Bioawareism #2 Biocontainment
- Creating a Culture of Care
- Dry Cow Management

### DairyCare365.com

"DAIRY CARE365 has helped our employees be more confident in their day-to-day tasks and has helped us take training to the next level." - CHRIS HEINS, HEINS FAMILY FARM, HIGGINSVILLE, MISSOURI

9/27/22 7:29 AM

# **PRODUCT INFORMATION**

#### ESTRUMATE<sup>®</sup> (cloprostenol injection)

ition of a prostaglandin F2 $\alpha$  analogue for intramuscular irv cows, and replacement beef and dairy heifers CAUTION: Federal (USA) law restricts this drug to use by or

Control recent (Co-A) and Estimate (Co-A) and Estimate (Co-A) constant injection) is a synthetic prostaglardin analogue structurally related to prostaglandin F2  $\alpha$  (PGF2  $\alpha$ ). Each mL of the sterile colorless aqueous solution contains 250 mcg doprostend (equivalent to 263 mcg doprostend berry/lachol, and water for injection, q.s.

INDICATIONS FOR LISE

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

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

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

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

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

Estrumate causes functional and morphological regression of the corpus luteum (luteolysis) in catile. In normal, non-pregnant cycling arimals, 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 (powerta, nummified texus, and luteal cycls), the induced luteolysis usually results in resolution of the condition and return to cyclicity. Pregnant animals may abort depending on the stage of gestation.

DOSAGE AND ADMINISTRATION: Two ml. of Estrumate (500 mcg cloprostenol) should b DUSAGE AND ADMINISTRATION: Wor The of Estrumate (500 mcg doprostenoi) should administered by INTRAMUSCULAR INJECTION using the specific dosage regimen for t indication. 20 mL bottle size: Use within 28 days of first puncture. 100 mL bottle size: U within 28 days of first puncture and puncture a maximum of 12 times. Use only with automa nrst puncture and puncture a maximum of 12 times. Use only tent or repeater syringe. Discard bottle after one stopper punct

On spins.
1. For unobserved or non-detected estrus in beef cows, lactating dairy cows, and replacement beef and dairy heffers. Cows and helfers which are not detected in estrus, although ovarian cyclicity continues, can be treated with Estrumate if a mature corpus luterm 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. Hestrus detection is not desirable prossible treated animals may be inseminated twice at about 72 and 96 hours post-injection.

For treatment of pyometra or chronic endometritis in beef cows, lactating dairy cows, and replacement beef and dairy heifers. Damage to the reproductive tract at calving or postpartum retention of the placenta often leads to interior epirotoxiter tidd: at kelving un endoted the placenta often leads to interior and inflammation of the uterus (endometrilis). Under certain circumstances, this may progress into chronic endometrilis with the uterus becoming distenced with puritient matter. This condition, commonly referred to as pometra, is characterized by a lack of cyclical estrous behavior and the presence of a persistent corpus betwen. Induction of lutelysis with Esturnate useably establish execution of the uterus and a return to normal cyclical activity within 14 days after teamment. After 14 days post-teament, recovery rate of treated animals will not be different than that of

3. For treatment of mummified fetus in beef cows, lactating dairy cows, and replace beef and dairy heifers. Death of the conceptus during gestation may be followed by i degeneration and dehydration. Induction of luteolysis with Estrumate usually results expulsion of the mummified fetus from the uterus. (Manual assistance may be necessary i n the vagina). Normal cyclical activity usually follow

4. For treatment of luteal cysts in beef cows, lactating dairy cows, and replacement beef and dairy heffers. A cow or heffer may be noncyclic due to the presence of a luteal cyst fail single, anovalustry follicit with a thickned wall which is accompanied by no external signs and by no changes in papable consistency of the uterus). Treatment with Strumate can restore normal ovarian activity by causing regression of the luteal cyst.

5. For abortion of beef cows, lactating dairy cows, and replacement beef and dairy heifers Unvanted pregnancies can be safely and efficiently terminated from 1 week after mating about 5 months of gestation. The induced abortion is normally uncomplicated and the and placenta are usually expelled about 4 to 5 days after the injection with the reproduced tract returning to normal soon after the abortion. The ability of Estrumate to induce ab decreases beyond the fifth month of gestation while the risk of dystocian and its consequence. lecreases beyond the fifth month of gestation while the risk of dystocia and its consequence ncreases. Estrumate has not been sufficiently tested under feedlot conditions; therefor ecommendations cannot be made for its use in heifers placed in feedlots.

6. For estrus synchronization in beef cows, lactating dairy cows, and replacement beef and dairy heffers. The luteolytic action of Estrumate can be utilized to schedule estrus and ovulation for an individual yocling animal or a group of animats. This allows control of the time at which cycling cows or heifers can be bred. Estrumate can be used in a breeding program with the following methods:

Single Estrumatering injection: Only animals with a mature corpus luteum should be treater to obtain maximum "searce to the single injection. However, not all cycling cattle should be treated single and an animal maximum searce to the single injection. However, not all cycling cattle should be treated single and animal maximum searce and the single injection. However, not all cycling cattle should be treated single and the single single corpus luteur is present for only 11 to 2 days of the 21-day cycle. Prior to treatment, cattle should be examined rectally and found to be anatomically normal, be non-pregnant, and have a nature corpus luteur. 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 latine following detection not estrus. If estrous detection is not desirable or possible, treated animals may be inseminated and 12 and 05 beinseminated and 12 and 05 beinseminated in the single interval and 12 and 05 beinseminated interval and 10 beinse either once at about 72 hours or twice at about 72 and 96 hours post-injection. With

enter force at about 7.2 hours or whole at about 7.2 and 96 hours post-enjection. While a single injection program, it may be desirable to assess the cyclicity status of the hear before Strumate treatment. This can be accomplished by heat detecting and breeding at the usual time following detection destrus for a 6-day period, all prior to injection. If by the sixth day the cyclicity status appears normal lapproximately 25%-30% detected in estrus, all cattle not already inseminated should be papated for normality, non-pregnancy, and cyclicity, then injected with Estrumate. Breeding should then be continued at the usual time following signs or destus 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 po injection) or on both the ninth and tenth days (at about 72 and 96 hours post-injection).

injectioný ór on both the ninfh and tenth days (at about 72 and 96 hours post-injection).
 Double Estrumate injections: prior to treatment, cattle should be examined rectally and found to be anatimically normal, non-pregnant, and cycling (the presence of a mature corpus lateum 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 21 to 5 days following the second Injection Should be given 11 days after the first injection. In normal, cycling cattle, estrus is expected 21 to 5 days following the second Istimust instead at the usual time following detection of estrus. If estrus detection is not desirable or possible, treated animals may be inseminated at the usad its following the second Estrumate injection. Many animalsvill come into estrus following the first injection, these animalscan be inseminated at the usual time following detection of estrus or any be inseminated should receive a second injection 11 days after the first injection. Animals receiving both injections may be inseminated explored the usual time following detection of estrus or any be inseminated end the usual time following detection of estrus or any be inseminated end the usual time following detection of estrus or any be inseminated end the usual time following detection factors may be inseminated end the usual time following detection destrus or any be inseminated end the usual time following detection destrus and use the inseminated end the usual time following detection destrus or any be inseminated end the usual time following detection destrus and use the inseminated end the usual time following detection destrus and use the inseminated at the usual time following detection destrus and use the inseminated end the usual time following detection destrus and use the inseminated end the usual time following detection destrus and use the inseminated end the usual time follo

commended should be completed by either: ecially during the third week after injection) and inseminating or Ils returning to estrus, or Any breeding program recomm observing animals (especially hand mating any animals retu

 turning in clean-up bull(s) 5 to 7 days after the last injection of Estrumate to cover any animals returning to estrus. Management considerations for use of Estrumate for estrus synchronization: A variety of programs can be designed to best meet the needs of individua systems. A breeding moraram should be selarated which is assessed to be

A variety of programs can be designed to best meet the needs of individual management systems. A breeding program should be selected which is appropriate for the existing circumstances and management practices. Before a breeding program is plannet, the producer's objectives must be examined and the producer must be made aware of the projected results and limitations. The producer and the consulting verteinnain should be view the operation's breeding history, herd health, and nutritional status and agree that b breeding program.

cows and heifers must be normal, non-pregnant, and cycling (rectal palpation should be performed); cows and heifers must be in sound breeding condition and on an adequate or increasing plane of nutrition;

proper program planning and record keeping are essential;

ust have occurred at least 5 days prior to treatments in the second structure of the second structure in the second structure is a second structure is a second structure in the second structure is a second structure is a second structure is a second structure is a second structure in the second structure is a second structure is

There is no difference in the facility achieved following the single or double dosage regimen when breeding occurs at induced estrus, or at 72 and 96 hours post-treatment. Conception rates may be lower than expected in those fixed time breeding programs employing Estrumate alone which omit the second insemination (ie, the insemination at or near 96 hours). This is especially true if a fixed time insemination is used following a single erform FTAI 8 to 24 hours after the second Fertagyl injection, or inseminate cows o pertered estructions standard berd practices For beef cows, the intramuscular dosage of Fertagyl is 86 mcg gonadorelin (2 mL) per cow, used n reproductive synchrony programs similar to the following: Administer the first Fertagyl injection (2 mL) on Day 0.

### For use with Fertagyl<sup>®</sup> (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows

Use in reproductive synchrony programs similar to the following: • Administer the first Fortagyl<sup>1</sup> injection (2 mL; 86 mcg gonadorelin, as gonadorelin acetate) by intramuscular injection on Davo.

WITHDRAWAL PERIODS AND RESIDUE WARNINGS: No milk

discard or pre-slaughter drug withdrawal period is required when used according to labeling. Use of this product in excess of the approved dose may result in drug residues.

USER SAFETY WARNINGS: Not for use in humans. Keep this and all drugs out of the reach

or children. Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. Estrumate is readily absorbed through the skin and can cause abortion and/or broncheapsms. Direct contact, with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water. Too btan copy of the Safety Data Sheet (DST) for trechnical assistance, contact Merck Animal Health at 1-800-211-5373 of http://www.merck.com

assistance, contact Merck Animal Health at 1-900-211-35/3 of http://www.merck.com ANIMAL SAFETY WARNINGS: As with all parenteral products, careful aseptic techniques should be employed to decrease the possibility of post-injection bacterial infection. Severe localized closificial infections associated with injection of Estrumate have been reported. In rare instances, such infections have resulted in death. Aggressive antibiotic therapy should be employed at the first sign of infection at the injection site, whether localized or diffuse. At 50 and 100 times the recommended dose, mild side factors may be detected in some cattle. These includes increased uncasiness, slight frothing, and milk let-down.

CONTACT INFORMATION: To report suspected adverse drug experiences, call Merck Animal Health at 1-800-211-357.3. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or at http://www.fda.gov/reportanimalae

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

Copyright © 2017 Intervet Inc (d/b/a Merck Animal Health) a subsidiary of Merck & Co., Inc. Madison, NJ 07940 All rights reserved.

For use with Estrumate (cloprostenol injection) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows

For use with cloprostenol sodium to synchronize estrous cycles to allow for FTAI in beef cows

**DESCRIPTION:** Fertagyl is a sterile solution containing 43 mcg/mL of gonadorelin (GnRH: as gonadorelin acetate) suitable for intramuscular or intravenous administration according to the indication Gonadorelin is a decapeptide composed of the sequence of animo acids – 5-com/t-His-Tip-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH<sub>2</sub> a molecular weight of 1182.32 and empirical formula c<sub>2</sub>H<sub>2</sub>H<sub>3</sub>H<sub>1</sub>/ $_{2}$ 

Gonadorelin is the hypothalamic releasing factor responsible for the release of gonadotropins (e.g., luteinizing hormone [LH], follicle stimulating hormone [FSH]) from the anterior pituitary. Synthetic gonadorelin is physiologically and chemically identical to the endogenous bovine hypothalamic releasing factor

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

HOW SUPPLIED: 20 mL and 100 mL multidose vials

STORAGE, HANDLING, AND DISPOSAL:

Approved by FDA under NADA # 113-645

FERTAGYL<sup>®</sup> (gonadorelin)

For treatment of cystic ovaries in dairy cattle

Conadorellin (as gonadorellin acetate) Benzyl Alcohol Sodium Chloride Water for Injection, USP pH adjusted with sodium phosphate (monobasic and dibasic).

43 mcg/mL gonadorelin Injectable Solution

Each mL of Fertagyl contains:

1. Protect from light. 2. Store in carton. 3. Store at 2-30°C (36-86°F).

Made in Germany Rev. 12/2018

WARNINGS AND PRECAUTIONS:

njection. Perform FTAI 0 to 24 hours after the second Fertagyl injection, or inseminate cows on

INGS AND PRECAUTIONS: Not for use in humans. Keep out of reach of children. WITHDRAWAL PERIODS: No withdrawal period or milk discard time is required when used according to the labeling.

, or report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Intervet at 1-800-211-3573. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or <u>http:// www.tdta.gov/ergortanimalac</u>

nister the second Fertagyl injection (2 mL) 30 to 72 hours after the cloprostenol sodiur

in oralies gyl is indicated for the treatment of ovarian follicular cysts in dairy cattle. Ovarian cyst non-ovulated follicles with incomplete luteinization which result in nymphomania o

Historically, cystic ovaries have responded to an exogenous source of LH such as human chorionic gonadotronin

tiates release of endorenous I H to cause ovulation and luteinizatio

Reproductive Synchrony Fertagyl is indicated for use with Estrumate (cloprostenol injection) to synchronize estrou cycles to allow for fixed time artificial insemination (FTA) in lactating dairy cows.

Fertagyl is indicated for use with cloprostenol sodium to synchronize estrous cycles to allow for FTAI in beef cows.

ysuc ovaries ne intravenous or intramuscular dosage of Fertagyl is 86 mcg gonadorelin (2 mL) per cow.

ed in repróductive synchrony programs similar to thé nister the first Fertagyl injection (2 mL) on Day O. nister 2 mL of Estrumate (500 mcg cloprostenol, as clop on 6 to 8 days after the first Fertagyl injection.

ntramuscular dosage of Fertagyl is 86 mcg gonadorelin (2 mL) pe chrony programs similar to the following:

nd Fertagyl injection (2 ml ) 30 to 72 hours after the Estrumate injection

MACOLOGY AND TOXICOLOGY. Endogenous gonadorelin is synthesized and/or def from the hypothalamus during various stages of the bovine estrous cycle following miste neurogenic stimuli. It passes in the hypothyseal portal vessels, to the anterior ry to effect the release of gonadotropins (e.g. LH, FSH). hetic gonadorelin administered intravenously or intramuscularly also genous LH or FSH from the anterior pituitary.

Gonadorelina cetate has been shown to be safe. The  $LD_{so}$  for mice and rats is greater than 60 mg/kg, and for dogs, greater than 600 mg/kg, respectively. No adverse effects were noted among rats or dogs administered 120 mg/kg/day or 72 mg/kg/day intravenously for 15 days.

It had no adverse effects on heart rate, blood pressure, or EKG to unanesthetized dogs at 60 mcg kg, In anesthetized dogs it did not produce depression of myocardial or system heardoynamic 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. Further, gonadorelin acetate did not cause irritation at the site of intramuscular administ n dogs with a dose of 72 mcg/kg/day administered for seven (7) days.

TARCET ANIMAL SAFETY: In addition to the animal safety information presented in the PHARMACOLOGY AND TOXICOLOGY section, the safety of gonadorelin was established through the review and evaluation of the extensive published literature available for the use of gonadorelin-containing products.

The intramuscular administration of 860 mcg gonadorelin (as gonadorelin acetate) on five (5) consecutive days to normally cycling dairy cattle had no effect on hematology or clinical

In field studies evaluating the effectiveness of gonadorelin for the treatment of ovarian follicular oysts, the incidence of health abnormalities was not significantly greater in cows administered gonadorelin than cows administered a placebo injection.

The target animal safety of, and injection site reactions to. Fertagyl when used with Estruma prostenci injection were evaluated during the conduct of effectiveness field studies tating dairy cows. The incidence of health abnormalities was not significantly greater wardinistrend learbard than own administrator a heapon injection. ess field studies i

The target animal safety of, and injection site reactions to, gonadorelin when used with decorrectand sodium were evaluated during the conduct of effectiveness field studies in bee cloprostenol sodium were evaluated during the conduct of effectiveness field stuc cows. The incidence of health abnormalities was not significantly greater in cows ad gonadorelin than cows administered a placebo injection.

EFFECTIVENESS: The use of gonadorelin for treatment of ovarian follicular cysts in dairy cattle was demonstrated to be effective with a treatment dose of 86 mcg gonadorelin (as

gonadorelin acetate). The effectiveness of Fertagyl for use with Estrumate (cloprostenol injection) to synchronize estrous cycles to allow for FIA 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 postpartimum were enrolled in the study. A total of 377 cows were administered Fertagyl (2 ml: 86 mcg gonadorelin as the acetate sait) and 381 cows were administered an equivalent volume of saline as an intramuscular injection twice in the following regiment:

Day 0: 2 mL Fertagyl or saline nol injection

Day 7: 2 mL Estrumate (clopro Day 9: 2 mL Fertagyl or saline

189979 R9

43 mcg 9 mg 7.47 mg q.s.

Fixed time AI was performed on Day 10, 16 ± 8 hours after the Day 9 injection. Cows we race unleave was perioritied on Da 43  $\pm$  5 days by trans-rectai 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 (17.3%).

(33.4%) than the pregnancy rate to FTAI to cowis treated with saline (17.8%). The effectiveness of gonadorelin for use with cloprostenol sodium to synchronize estruus cycles to allow for FTAI in beef cows was demonstrated in a field study at 10 different locations in the U.S. Atotalo 1706 healthy, non-pregnant, miniparous are for hubiparous beef conversioned days postparture were enrolled in the study. Atotal of 384 cows were administered gonadorelin (1 mL, 100 mog gonadorelin as the acates all) and 342 cows were administered an equivalent volume of water for injection as an intramuscular injection wice in the following regiment:

Day 0: 100 mcg gonadorelin (as the acetate salt) or sterile water for injection Day 7: 500 mcg cloprostenol (as cloprostenol sodium) Day 9: 100 mcg gonadorelin (as the acetate salt) or sterile water for injection

Fixed time AI was performed immediately after the Day 9 injection. Cows were evaluated for pregnancy on Day 55±5 days by trans-rectal ultrasound. Pregnancy rate to FTAI was

significantly higher (P=0.0006) in cows treated with gonadorelin (21.7%) than the pregnancy rate to FTAI in cows treated with water (7.4%).

The effectiveness of a 2-mL dose of gonadorelin delivering 86 mcg gonadorelin (as gonadorelin acetate) for use with cloprostenol sodium to synchronize estrous cycles to allow for TFJA in lactating dairy cows and beef cows was also demonstrated through references to scientific literature. HOW SUPPLIED: Fertagyl is available in a concentration of 43 mcg/mL gonadorelin (as gonadorelin acetate) of adjusted with sodium phosobate (monobasic and dibasic).

Fertagyl is supplied in multi-dose vials containing 20 mL and 100 mL of sterile solution STORAGE, HANDLING, AND DISPOSAL: Keep refrigerated: 2\*.8\*C (36\*.46\*F).

20 mL vial: Use within 28 days of first puncture.

100 mL viail. Use within 28 days of first puncture and puncture a maximum of 10 times when using an 18 gauge needle. When using a draw-off spike or needle with bore diameter large than 18 gauge, discard any product remaining in the vial immediately after use. Approved by FDA under ANADA # 200-134

MANUFACTURED FOR: Intervet Inc. (d/b/a Merck Animal Health). Madison. NJ 07940

Gonadorelin (active ingred.) made in the Netherlands. Formulated in Germany.

Copyright @2020 Intervet Inc. (d/b/a Merck Animal Health), a subsidiary of Merck and Co., Inc. All rights reserved Rev. 02/2020

### **CHORULON°**

Intervet/Merck Animal Health 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 

ACTION: Chorionic gonadotropin has luteinizing hormone-like activity with little or no follicle stimulating or estrogenic activity. INDICATIONS: COWS: CHORULON<sup>®</sup> is indicated for intramuscular use in cows for the treatment of nymphomania (frequent or constant head) due to cystic ovaries.

FINFISH: CHORULON® is indicated for use as an aid in improving spawning function in male 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<sup>®</sup> contains 10,000 I.U. chorionic gonadotropin.

COWS: The contents of one vial (10 mL) of reconstituted CHORULON<sup>®</sup> 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.

behavior or rectal examination of the ovalines indicates the necessary for ferenament. INHSR: 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 does of 50 to 510 LUJb body venight (bw) for males and 67 to 1816 LUJb bw for females. Depending on body weight and dose administered, it may be necessary to divide the does among two or more injection sites to avoid injecting a large INS15427.03 plume at a single site.

volume at a singure site. Summaries of doses tested in representative fish species are contained within the following tables. The dose of CHORULON<sup>4</sup> to be used in other species of finitish may differ from those snecies listed in the tables, but should fall within the suggested range of 50 to 510 LU.Jb bw fo species listed in the tables, but should fall w males and 67 to 1816 I.U./Ib bw for females

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

able 2. Tested Fish Species/Dose Combination	ons Found to	be Safe			
Nomenclature Common Name, Genus & Species, Family	Tested (I.U./Ib bw	Dose(s) /injection)	Number of Injec-	Injec- tion	
	Males	Females	uons	(h)	
white bass, <i>Morone chrysops</i> , Percichthyidae	750	1500	1	-	
walleye, Stizostedion vitreum, Percidae	750	1500	1	-	
grass carp, Ctenopharyngodon idella,	2500	5000	1		

Cynrinidae channel catfish, *Ictalurus punctatus*, 2500 5000 lctaluridae 1 ADVERSE REACTIONS: Chorionic gonadotropin is a protein. In the unlikely event of an ananhylactic reaction. epinephrine should be administered. The administration of an anaphylactic reaction, epinephini antihistamine may also be indicated

antinistamine may also be indicated. **RESIDUE WARNINGS:** No withdrawal period is required for cows or brood finfish treated according to label directions. The total does administered all injections combined) should not exceed 25,000 LU (25 mL) per fish in fish interded for human consumption. **STORAGE AND HANDLING PRECAUTIONS:** Store at or below room temperature, 77°F (25°C). Keep out of reach of children. Once recordsituted, 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 source and five 10 ml vials of sterile filluent. Order Code No. CH-475-1.

intervet Inc., a subsidiary of Merck & Co. Inc., Summit, NJ 07901 USA hy: Intervet International GmbH Unterschleissheim Germany

Rev. 4/14 142021 R2 CPN: 1047314.2

body weight (BW). Do not inject more than Table 1. AROVYN Cattle Dosing Guide Animal Weight 100 200

49

us citric acid, 6.7 mg sodium chloride, 20 mg

.. n-detected estrus in beef cows. lactating dairy cows. and replacement

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

Administer 500 mcg cloprostenol (as cloprostenol sodium) by intramuscular injection 6 to 8 days after the first Fertagyl injection.

Administer 2 mL of Estrumate by intramuscular injection 6 to 8 days after the first <sup>S</sup>ertagy<sup>®</sup> injection.

 Administer the second Fertagyl<sup>®</sup> injection (2mL; 86 mcg gonadorelin, as gonadorelin acetate) 30 to 72 hours after the Estrumate injection. acetate) 30 to 72 hours after the Estrumate injection. • Perform FTAI 8 to 24 hours after the second Fertagyl® injection, or inseminate cows on TRAINDICATIONS: Do not use this drug product in pregnant cattle, unless abortion is desired.

DOSAGE AND ADMINISTRATION: Cystic Ovaries

Reproductive Synchrony For lactating dairy cows, the in cow, used in reproductive syn

#### AMOXI-MAST<sup>®</sup> (amoxicillin intramammary infusion) LACTATING COW FORMULA

#### ntramammary Infusion

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinaria Amoxi-Mast (amoxicillin intramammary infusion) 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.

manufactured by a nonstenilizing process. Amoxicillin trihydrate is a semisynthetic penicillin derived from the penicillin nucleus, 6-amino-penicillanic acid. Chemically, Iti s0(4)-x-amino-p-hydroxyberzyl penicillin trihydrate. ACTION: Amoxicillin trihydrate is bactericidal in action against susceptible organisms. It is a broad-spectrum antibiotic which is effective against common infectious mastifis pathogens, namely Streptococcus agalactiae and penicillin-sensitive Staphylococcus aureus.

with the states of the states and th

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.

WARNINGS: Milk taken from animals during treatment and for 60 hours (2.5 days) 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 preservamines)

the subject should be treated with the usual agents (antihistamines, pressor amures). DOSAGE AND ADMINISTRATION: Milk out udder completely. Wash udder and teats the couple wath wath water water containing a suitable dairy antiseptic. Dry thoroughly. Clean and 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 onfice. Express the superaion into the quarter will gentle and continuous pressure. Withdraw the syringe and grasp the end of the teat firmly age the medication up into the milk cistern.

For optimum response, the durg 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

teatornice. HOW SUPPLIED: Amoxi-Mast is supplied in cartons of 12 single-dose syringes with 12

alcohol swabs. Each 10-mL, disposable syringe contains am 62.5 mg of amoxicillin activity. o Not Store Above 24°C (75°F)

NADA #55-100, Approved by FDA Manufactured by

G.C. Hanford Mfg. Co. Syracuse, NY 13201

© 2015 Intervet Inc., a sub Madison, NJ 07940, USA. All rights reserved. 02/18 idiary of Merck & Co., Inc



### **AROVYN**<sup>®</sup>(tulathromycin injection)

00 mg of tulathromycin/m

For use in beef cattle (including suckling calves), non-lactating dairy cattle (including dairy calves), veal calves, and swine. Not for use in female dairy cattle 20 months of age or older. CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian CAD INFORCEDUATION CONTRICT AND A CONTRIPACT AND A CONTRICT AND A CONTRICT AND A



The chemical names of the isomers are (2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[[2.6-dideoxy-3-C-methyl-4-C-[propylamino]methyl]-e-L-ribo-hexopyranosyl[oxy] -2-ethyl-34, 10-rihydroxy-3-58,10,12,14-hexamethyl-11-[3.6-trideoxy-3-C(idmethy-lamino]+D-xylo-hexopyranosyl[oxy]-1-oxa-6-zezv[dopentadecan-15-one and (2R, 3R, 6R, 8R, 9R, 10S, 115, 12R)-11-[[2.6-dideoxy-3-C-methyl-4-C-[propylamino]methyl]-a-L-ribo-hexopyranosyl[oxy]-2, [1R,2R)-1, 2-didydroxy-1-methyl-hyl]-8-hydroxy-3, 68, 61, 01-2 pertinatehyt-9-[13,64-trideoxy-3-didmethylamino]+D-xylohexopyranosyl[oxy]-1-oxa-4- azacyclotridecan-13-one, respectively.

INDICATIONS: Beef and Non-Lactating Dairy Cattle BRD - AROVYN Injectable Solution is indicated for the treatment of bovine respiratory BID – AROVI'III injectable Solution is indicated ion the dealinent of both respiratory disease (BRO) associated with Mannheimia haemotylica, Pasteurella multocida, Histophilus somni, and Mycoplasma bovis; and for the control of respiratory disease in cattle at high risk of developing BRD associated with Mannheimia haemotylica, Pasteurella

IBK – AROVYN Injectable Solution is indicated for the treatment of infectious bovine keratoconjunctivitis (IBK) associated with *Moraxella bovis*. Foot Rot – AROVYN Injectable Solution is indicated for the treatment

Suckling Claves, Dairy Calves, and Veal Calves RRD - AROVYN Injectable Solution is indicated for the treatment of BRD associated with M.

Ivtica. P. multocida. H. somni. and M. bovis

Swine AROVYN Injectable Solution is indicated for the treatment of swine respiratory disease SROJ associated with Actinobacillus pleuropneumoniae, Pasteurella multicida, Bordetella bronchiseptica, Haemophilus parasuis, and Mycoplasma hyponeumoniae, and for the control of SRD associated with Actinobacillus pleuropneumoniae, Pasteurella multicida, and Mycoplasma hyponeumoniae in groups of pigs where SRD has been diagnosed. SAGE AND ADMINISTRATION

subcutaneously as a single dose in the neck at a dosage of 2.5 mg/kg (1.1 mL/100 lb) weight (BW). Do not inject more than 10 mL per injection site.

(Pounds)	Dose Volume (mL)	Animal Weight (Pounds)	Dose Volume (mL)
	1.1	600	6.8
	2.3	700	8.0
	3.4	800	9.1
	4.5	900	10.2
	57	1000	11.4

Swine Inject intramuscularly as a single dose in the neck at a dosage of 2.5 mg/kg (0.25 mL/22 lb) BW. Do not inject more than 2.5 mL per injection site. Table 2. AROVYN Swine Dosing Guide

Animal Weight (Pounds)	Dose Volume (mL)	Animal Weight (Pounds)	Dose Volume (mL)
15	0.2	170	1.9
30	0.3	190	2.2
50	0.6	210	2.4
70	0.8	230	2.6
90	1.0	250	2.8
110	1.3	270	3.1
130	1.5	290	3.3
150	17		

CONTRAINDICATIONS: The use of AROVYN Injectable Solution is contraindicated in animals previously found to be hypersensitive to the drug. WARNINGS: FOR USE IN ANIMALS ONLY. NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. NOT FOR USE IN CHICKENS OR TURKEYS.

#### RESIDUE WARNINGS:

Cattle Cattle intended for human consumption must not be slaughtered within 18 days from the last treatment. This drug is not approved for use in female dairy cattle 20 months of age or older, including dry dairy cons. Use in these cattle may cause drug residues in milk and/or in calves born to these cows.



Swine intended for human consumption must not be slaughtered within 5 days from the last treatment

#### PRECAUTIONS

Cattle The effects of AROVYN not been determined. The effects of AROVYN on bovine reproductive performance, pregnancy, and lactation have not been determined. Subcutaneous injection can cause a transient local tissue reaction that may result in trim loss of edible tissue at slaughter.

Swine The effects of AROVYN on porcine reproductive performance, pregnancy, and lactation have not been determined. Intramuscular injection can cause a transient local tissue maction that may result in trim loss of edible tissue at slaughter. DVFRSE REACTIONS

Cattle In one BRD field study, two calves treated with tulathromycin injection at 2.5 mg/kg BW exhibited transient hypersalivation. One of these calves also exhibited transient dyspnea, which may have been related to pneumonia.

Swine In one field study, one out of 40 pigs treated with tulathromycin injection at 2.5 mg/kg BW exhibited mild salivation that resolved in less than four hours.

Post APPROVAL EXPERIINCE: The following adverse events are based on post approval adverse drug experience reporting. Not all adverse events are reported to the FDA CVM. It is not always possible to reliably estimate the adverse events are reported to the FDA CVM. It is not always possible to reliably estimate the adverse events are reported to the FDA CVM. It is not always possible to reliably estimate the adverse events are reported to the FDA CVM. It adverse and the reliably estimate the adverse events are reported to the FDA CVM. It is not always possible to reliably estimate the adverse events are listed in decreasing order of reporting frequency in cattle: injection site reactions for anaphylaxic anaphylactotic reactions. For a complete listing of adverse reactions for tulathormycin injectable solution reported to the CVM see: <u>http://www.fda.gov/reportanimalae</u>.

CLINICAL PHARMACOLOGY: At physiological pH, tulathromycin (a weak base) is approximately 50 times more soluble in hydrophilic than hydrophobic media. This solubility approximately 50 times more soluble in hydrophilic than hydrophobic media. This solubility profile is consistent with the extracellular pathogen activity hydrophosity associated with the macrolides.<sup>1</sup> Markedly higher tulathromyon concentrations greenest free factived drug was not examined. Therefore, the clinical relevance of these elevated lung concentrations represent free factived drug undetermined. Although the relianship between tulathromyon and the characteristics of its antiderismical Although the relianship between tulathromyon and the characteristics of the antiderismical through the number of these elevated lung concentrations re-busting estimation and the source of these elevated lung concentrations is antimicrobial effects has not been characterized, as a class, macrolides tend to be primarily between the may be between attemports. antimicrobial effects has not been characterized, as a class, macrolides tend to be primarily bacteriostatic, but may be bactericidal againts come pathogens.<sup>27</sup> They also tend to exhibit concentration independent killing; the rate of bacterial eradication does not change once serum drug concentrations reach 2 to 3 times the minimum inhibitory concentration (MC) of the targeted pathogen. Under these conditions, the time that serum concentrations remain above the MC becomes the major determinant of antimicrobial activity. Macrolides also exhibit a post-antibiotic effect (PAC), the duration of which tends to be both drug and pathogen dependent. In general, by increasing the macrolide concentration and the exposure time, the PAE will increase to some maximal duration. Of the two variables, concentration of PAE. Tulathromycin is eliminated from the body primarily unchanged via bilary excertion.

<sup>1</sup>Carbon, C. 1998. Pharmacodynamics of Macrolides, Azalides, and Streptogramins: Effect on Extracellular Pathogens. Clin. Infect. Dis., 27:28-32. <sup>a</sup>Nightingale, C.J. 1997. Pharmacokinetics and P harmacodynamics of Newer Macrolides. Pediatr. Infect. Dis. J., 16:438-443.

#### Cattle

Cattle Following subcutaneous administration into the neck of feeder calves at a dosage of 2.5 mg/ kg Wk tulathromycin is rapidly and nearly completely absorbed. Peak plasma concentrations generally occur within 15 minutes after dosing and product relative bioavailability exceeds 90%. Total systemic clearance is approximately 170 mL/hr/kg. Tulathromycin distributes extensively into body tissues, as evidenced by volume of distribution values of approximately responsible for the long elimination hall-life of this compound [approximately 2.75 days in the plasma [dused on quantifiable terminal plasma drug concentrations) eversus 8.75 days for total lung concentrations (based on data from healthy animals)]. Linear pharmacokinetic are observed with subcutaneous doses ranging from 12.7 mg/kg BW to 5.0 mg/kg BW. No pharmacokinetic differences are observed in castrated male versus female calves.

Clearance and volume estimates are based on intersubject comparisons of 2.5 mg/kg BW administered by either subcutaneous or intravenous injection.

Swine Following intramuscular administration to feeder pigs at a dosage of 2.5 mg/kg BW, tothermucin is completely and ranidly absorbed (T<sub>max</sub> 0.25 hour). Subsequently, the drug Following intramuscular administration to beder pigs at a dosage of 2.5 mg/kg BW, tulatimomycin is completely and regitaly absorbed [1] mm, O25 hours, Subsequently, the drug rapidly distributes into body tissues, achieving a volume of distribution exceeding 15 L/kg. However, It has a long terminal elimination half-file (60 or 50 hours) owing to its extensive volume of distribution. Although uplinomary tulation myclic or 50 hours) owing to its extensive is undetermined. There are no general reflectione distributions are substantially higher than concentration distributed reflections and using tulations distributions and these informations and is undetermined. There are no general reflections and using tulations parameters and the set of these informations and the substantially is undetermined. MICROBIOLOGY:

Cattle Tulathromycin has demonstrated in vitro activity against Mannheimia haemolytica, Pasteurella multocida, Histophilus somni, and Mycoplasma bovis, four pathogens associated with BRD; against Morazella bovis associated with HbK; and against Fusobacterium necrophorum and Porphyromonas levii associated with bovin foot rot.

The MICs of tulathromycin against indicated BRD and IBK pathogens were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLSI, M31-A2). The MICs against foot rot pathogens were also determined using methods recommended (M11-A6). All MIC values were determined using the 9:1 isomer ratio of this compour

(M11-46), All MIL Values were determined uang the ½1 somer ratio of this compound. BRD - The MICs of flukthromychin were determined for RBD isolates obtained from calves enrolled in therapeutic and at-ick field studies in the U.S. in 1999. In the therapeutic studies, isolates were obtained from pretextment nacopharyngel avable from all study calves, and from lung snabs or lung tissue of saline-treated calves that died. In the at-risk studies, isolates were obtained from nasopharyngeal snabs for all study calves, and from lung snabs or lung tissue of saline-treated calves that died. The results are shown in Table 3.

BRK - The MICS of tulathromycin were determined for *Moraxella* bovis isolates obtained from calves enrolled in IBK field studies in the U.S. in 2004. Isolates were obtained from per-treatment conjunctival avaiso 6 calves with clinical signs of IBK enrolled in the ulathromycin injection-treated and saline-treated groups. The results are shown in Table 3.

Foot Rot – The MICs of tulathromycin were determined for *Fusobacterium necrophorum* and *Pophyromonas levi* obtained from cattle enrolled in foot rot field studies in the US. and Canada in 2007. Isolates were obtained from perteatment interdigital biopsies and swabs of cattle with clinical signs of foot rot enrolled in the tulathromycin injection-treated and saline-treated groups. The results are shown in Table 3.

AROVYN con't next page

AROVYN con't

Table 3. Tulathr

Indicated pathogen	Date isolated	No. of isolates	MIC <sub>50</sub> ** (ug/mL)	MIC <sub>90</sub> ** (ug/mL)	MIC range (ug/mL)
Mannheimia haemolytica	1999	642	2	2	0.5 to 64
Pasteurella multocida	1999	221	0.5	1	0.25 to 64
Histophilu somni	1999	36	4	4	1 to 4
Mycoplasma bovis	1999	43	0.125	1	$\leq 0.063  to > 64$
Moraxella bovis	2004	55	0.5	0.5	0.25 to 1
Fusobacterium necrophorum	2007	116	2	64	$\leq 0.25to > 128$
Porphyromonas levii	2007	103	8	128	$\leq 0.25to > 128$
Porphyromonas levii	2007	103	8	128	$\leq 0.25$ to > 1

\* The correlation between in vitro susceptibility data and clinical effectiveness is unkr \* The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respect Swine In vitro activity of tulathromycin has been demonstrated against Actinobacillus pleuropneumoniae, Pasteurella multocida, Bordetella bronchiseptica, Haemophilus parasuis, and Mycoplasma hyopneumoniae. The MCs of tulathromycin against indicated the superscription of the superscription of the superscription of the superscription. pleuropneumonae, resseurcea manaceaster The MCs of tulathromycin against inducateu parasuis, and Mcyoplasma hypopeniumoniae. The MCs of tulathromycin against inducateu SRD pathogens were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLS), M31 A and M31-A3), MCS of Haemophilus parasuis termined using Veterinary Fastildious Medium and were incubated up to 48 hours Laboratory Standards Institute (CLSI, M31-4 and M31-A3), MICs for *Haemophilus parasus* were determined using Vterinary Fsätidious Medium and were inclusted up to 48 hours at 35 to 37°C in a CO2-enriched atmosphere. All MIC values were determined using the 9:1 isomer ratio of this compound. Isolates obtained in 2000 and 2002 were from lung samples from saline-treated pigs and non-treated sentinel pigs enrolled in Treatment of SRD field studies in the U.S. and Canada. Isolates obtained in 2007 and 2008 were from lung samples from saline-treated and tulathroung in injection-treated pigs enrolled in the Control of SRD field study in the U.S. and Canada. The results are shown in Table 4.

Table 4. Tulathromycin minimum inhibitory concentration (MIC) values\* for indicated pathogens isolated from field studies evaluating SRD in the U.S. and Canada.

Indicated pathogen	Date isolated	No. of isolates	MIC <sub>50</sub> ** (ug/mL)	MIC <sub>90</sub> ** (ug/mL)	MIC range (ug/mL)
Actinobacillus pleuropneumonia	2000-2002 2007-2008	135 88	16 16	32 16	16 to 32 4 to 32
Haemophilus parasuis	2000-2002	31	1	2	0.25 to > 64
Pasteurella multocida	2000-2002 2007-2008	55 40	1 1	2 2	$\begin{array}{c} 0.5 \ to > 64 \\ \leq 0.03 \ to > 2 \end{array}$
Bordetella bronchiseptica	2000-2002	42	4	8	2 to 8

\* The correlation between in vitro susceptibility data and clinical effectiveness is unkr \*\* The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respect EFFECTIVENESS:

EFFECTIVENESS: Cattle BRD - In a multi-location field study, 314 calves with naturally occurring BRD were treated with tulathromycin injection. Responses to treatment were compared to saline-treated controls. A cure was defined as a calf with normal attitude/activity, normal respiration, and a rectal temperature of < 104 <sup>+</sup> fon Day 14. The cure rate was significantly higher (P ≤ 0.05) in tulathromycin injection-treated calves (78%) compared to saline-treated calves (24%). There were two BRD-related deaths in the tulathromycin injection-treated calves compared to nine BRD-related deaths in the calves.

Fifty-two tulathromycin injection-treated calves and 27 saline-treated calves from the multi-location field BRD treatment study had Mxcanlasma hous identified in outputs from munu-rocanom neu okou treatment study had *Mycoplasma bovis* identified in cultures for pre-treatment nasopharyngeal swabs. Of the 52 tulathromycin injection-treated calve 37 (71.2%) calves were categorized as cures and 15 (28.8%) calves were categorized treatment failures. Of the 27 saline-treated calves, 4 (14.8%) calves were categorized cures and 23 (85.2%) calves were treatment failures.

cures and 23 (85.2%) calves were treatment failures. A Bayesian meta-analysis was conducted to compare the BRD treatment success rate in young calves (calves weighing 250 lbs or less and fed primarily a milk-based diet) treated with tulathromycin injection to the success rate in dider calves (calves weighing more than 250 lbs and fed primarily a roughage and grain-based diet] treated with tulathromycin injection. The analysis included data from four BRD treatment effectiveness studies conducted for the approval of tulathromycin injection in the U.S. and nine contemporaneous studies conducted in Europe. The analysis showed that the BRD treatment success rate in older calves. As a result, tulathromycin injection is considered effective studies calves. As a result, tulathromycin injection is considered effective success rate in order carves. As a result, unarmomycin injection is considered enective for the treatment of BRD associated with *M. haemolytica*, *P. multocida*, *H. somni*, and *M. bovis* in suckling calves, dairy calves, and veal calves.

In another multi-location field study with 399 calves at high risk of developing BRD. In another multi-location held study with 399 calves at high risk of developing BKU administration of tubathromycin injection resulted in a significantly reduced incidence of BRD (11%) compared to saline-treated calves (59%). Effectiveness evaluation was based on scored clinical signs of normal attitudelativity, normal respiration, and a recta temperature of < 104°F on Day 14. There were no BRD-related deaths in the saline-treated calves (59%). Effectiveness relations with the saline-treated calves compared to two BRD-related deaths in the saline-treated calves (59%) and *Al Mycoplasma boxis* identified in cultures of post-treatment nasopharyngeal swabs or lung tissue.

identified in cultures of post-treatment nasopharyngeal swabs or iung tssue. Two induced infection model studies were conducted to confirm the effectiveness of tulathromycin injection against *Mycoplasma bovis*. A total of 166 calves were inoculated intratracheally with field strains of *Mycoplasma bovis*. When calves became pyrexic and thad abnormal respiration scores, they were treated with either tulathromycin injection (2.5 mg/kg BW) subcutaneously or an equivalent volume of saline. Calves were observed for signs of BR0 for 14 days post-treatment, then were euthanized and necropsied. In both studies, mean lung lesion percentages were statistically significantly lower in the tulathromycin injection-reated calves compared with saline-treated calves (11.3% x 29.9%, P = 0.0001 and 15.0% vs. 30.7%, P < 0.0001).

IRK - Two field studies were conducted evaluating tulathromycin injection for the treatment IBK - Two field studies were conducted evaluating tulathromycin injection for the treatment of IBK associated with Morazeld aboxin 2000 anturally-infected cabuses. The primary clinical endpoint of these studies was cure rate, defined as a calf with no clinical signs of IBK and no corneal ulcer, assessed on Days 5, 9, 13, 17, and 21. Time to improvement, defined as the first day on which a calf had no clinical signs of IBK in both reyes, provided that those scores were maintained at the next day of observation, was assessed as a secondary variable. At all time points, in both studies, the curre rate was significantly higher (P < 0.05) for tulathromycin injection-treated cables compared to saline-treated cables. Additionally, time to improvement was significantly less (P < 0.0001) in both studies for curre treated cables.</p>

Injection-related carves compared to 20simil-related carves. Foot Ret – The effectiveness of tulathromycin injection for the treatment of bovine foot rot was evaluated in 170 cattle in two field studies. Cattle diagnosed with bovine foot rot were enrolled and treated with a single subcuraneous dose of fulathromycin injection (2.5 mg/kg BW) or an equivalent volume of saline. Cattle were clinically evaluated 7 days after treatment for treatment success, which was based on defined decreases in lesion, swelling, and lameness scores. In both studies, the treatment success percentage was statistically significantly higher in lulathromycin injection-treated calves compared with atistically significantly higher in tulathromycin injection-treated calves compa line-treated calves (60% vs. 8%, P < 0.0001 and 83.3% vs. 50%, P = 0.0088).

Swine In a multi-location field study to evaluate the treatment of naturally occurring SRD, 266 pigs were treated with tulathromycin injection. Responses to treatment were compared to saline-treated controls. Success was defined as a pig with normal attitude, normal respiration, and rectal temperature of < 104F on Day 7. The treatment success rate was Initiantly greater ( $P \le 0.05$ ) in tulathromycin injection-treated pigs (70.5%) compared saline-treated pigs (46.1%). *M. hyopneumoniae* was isolated from 106 saline-treated d non-treated sentinel pigs in this study.

and non-treated sentinel pigs in this study. Two induced inflection nodel studies were conducted to confirm the effectiveness of tulathromycin injection against *M. hyppneumoniae*. Ten days after inoculation intranasally and instratrocheally with a field strain of *M. hyppneumoniae*. 144 pigs were treated with either tulathromycin injection (2.5 mg/kg BW) intramuscularly or an equivalent volume of saline. Pigs were euthanized and necropsied 10 days post-treatment. The mean percentage of gross pneumonic lung lesions was statistically significantly lower (P < 0.0001) for tulathromycin injection-treated pigs than for saline-treated pigs in both studies (8.52% vs. 23.62% and 11.31% vs. 26.42%). The affordment of tubathromycin lineation is the northout of SDD was environted in a an equivalent volume of saline. Pigs were euthanized and necrosifed 10 days statistically significantly lower (P < 0.0001) for tulathrowyni nijection-treated pigs in both studies (8.52% vs. 23.62% and 11.31% vs. 26.42%). The effects of the control of SBD was evaluated in a multi-location natural infection field study. When at least 15% of the study candidates

51

 

 Tulathromycin minimum inhibitory concentration (MIC) values\* for indicated from field studies evaluating BRD and IBK in the U.S. and from foor to its in the U.S. and from foor the U.S. and from foor the its in the U.S. and from foor the U. ANIMAL SAFETY:

Cattle Safety studies were conducted in feeder calves receiving a single subcutaneous dose of 25 mg/kg BW, or 3 weekly subcutaneous doses of 2.5, 7.5, or 12.5 mg/kg BW. In all or 25 mg/kg BW, or 3 weekly subcutaneous doese of 2.5, 7.5, or 12.5 mg/kg BW. In all groups, transient indications of pain after injection were seen, including head shaking and pawing at the ground. Injection site swelling, discoloration of the subcutaneous tissues at the injection site and corresponding histopathologic changes were seen in animals in all dosage groups. These lesions were observed macroscopically or microscopically.

reams were user reamsuscipation in conception. This issues of the series of the series

A safety study was conducted in preruminant calves 13 to 27 days of age receiving 2.5 mg/ kg BW or 7.5 mg/kg BW once subcutaneously. With the exception of minimal to mild injection site reactions, no drug-related clinical signs or other lesions were observed macroscopically

Swine Safety studies were conducted in pigs receiving a single intramuscular dose of 25 mg/ kg BK, or 3 weekly intramuscular doses of 2.5, 7.5, or 1.25, mg/kg BW. In all groups, transient indications of pain after injection were seen, including restlements and excessive vocalization. Tremors occurred briefly in one animal receiving 7.5 mg/kg BW. Discoloration and edema of injection site tissues and corresponding histopathologic change were seen in animals at all dosages and resolved over time. No other drug-related lesions were observed animals were observed. vically or microscopically.

macroscopically or microscopically. **STORAGE CONDITIONS:** Store below 30°C (86°F), with excursions up to 40°C (104°F). Use this product within 84 days of the first puncture and puncture a maximum of 20 times. If more than 20 punctures are anticipated, the use of automatic injection equipment or a repeater syninge is recommended. When using a draw-off site or needle with bore diameter larger than 16 gauge, discard any product remaining in the vial immediately after use.

HOW SUPPLIED: AROVYN Injectable Solution is available in the following package sizes: 50 mL vial, 100 mL vial, 250 mL vial, and 500 mL vial

Approved by FDA under ANADA # 200-715 Tulathromycin (active ingred.) made in China. Formulated in Germany.

Distributed by Intervet Inc, (d/b/a Merck Animal Health), Madison, NJ 07940

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Merck Animal Health at 1-800-211-3573. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <u>http://www.FDA.</u>



#### **RESFLOR GOLD**<sup>®</sup> (florfenicol and flunixin meglumine) NADA 141-299, Approved by FDA. Antimicrobial/Non-Steroidal Anti-Inflammatory Drug

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 antiinflammatory drug (NSAID) flumkin. Each milliliter of sterile RESFLOR GOLD\* contains 300 mm glinfernicol, 16.6 mg flunkin as flunkin meglumine, 300 mg 2-pyrrolidone, 35 mg malic acid, and triacetin qs.

2-pyrrolidone, 35 mg malic acid, and triacetin qs. INDCATION: RESFLOR GOLD<sup>6</sup> is indicated for treatment of bovine respiratory disease (BRD) associated with Mannheimia haemolytica, Pasteurella multocida, Histophilus somi, and Mycoplasma bovis, and control of BRD-associated pyrexia in beef and non-lactating dairy cattle. DOSAGE AND ADMINISTRATION: RESFLOR GOLD<sup>6</sup> should be administered once by subcutaneous injection at a dose rate of 40 mg forfenicol/kg body weight and 2.2 mg flunkin/ kg body weight (6 mL/100 lb). Do not administer more than 10 mL at each site. The nijection 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.



CONTRAINDICATIONS: Do not use in animals that have shown hyper or flunixin.

WARNINGS: NOT FOR HUMAN USE, KEEP OUT OF REACH OF CHILDREN. This product 

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.

assistance of orleptor subjective adverse relacions, cain 1-000-219-2260. **PRECAUTIONS:** As a class, cyclo-oxygenase inhibitory ISAIDs may be associated with gastointestinal, 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 dephydrated, on duriet therapy, or those with existing renal, cardiovacular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully monitored INSAID may individual prostandantism the maintain comments. dystunction. Loncurrent administration of potentially nephrotoxic drugs should be carefully monitored. NSADs may inhibit the prostagalandis that maintain normal homeestalic 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 NSADs possess the potential to produce gastrointestinal ulceration, concommant use of RSFLOR 600L<sup>1</sup> with other anticificant administration data such as NSADs or corticosteroids, should such as the su

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 may occur with its use. I he most mequently 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.

have not been evaluated in a controlled study. NSAIDs are known to have the p parturition through a tocolytic effect. RESFLOR GOLD<sup>9</sup>, 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.



ADVERSE REACTIONS: Transient inappetence, diarrhea, decreased water consumption and injection site swelling have been associated with the use of florfenicol in cattle. In addition, anaphytaxis and collapse have been reported post-approval with the use of anothe 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<sup>®</sup> 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 <sub>0-t</sub> <sup>1</sup> (ng*hr/mL)	AUC <sub>0-inf</sub> <sup>2</sup> (ng*hr/mL)	C <sub>max</sub> <sup>3</sup> (ng/mL)	T <sub>max</sub> <sup>4</sup> (hr)	T <sub>1/2</sub> <sup>5</sup> (hr)	MRT <sub>0-inf</sub> <sup>6</sup> (hr)
Mean	242527	247577	11151	6.25	28.5	27.3
SD <sup>7</sup>	42741	41391	4194	3.87	9.91	11.6
ble 2. Mean (n=28) pharmacokinetic parameters for flunixin in cattle after a single bottaneous administration of RESELOR GOLD (flunixin dose of 2.2 mo/kg BW)						

Mean Flunixin PK parameters in Cattle

PK Parameter	AUC <sub>0-t</sub> 1 (ng*hr/mL)	AUC <sub>0-inf</sub> <sup>2</sup> (ng*hr/mL)	C <sub>max</sub> <sup>3</sup> (ng/mL)	T <sub>max</sub> <sup>4</sup> (hr)	T <sub>½</sub> <sup>5</sup> (hr)	MRT <sub>0-inf</sub> (hr)	
Mean	13370	14448**	1913	1.14	9.5**	11.4	
SD7	4964	5116	701	0.97	3.27	4.41	l

-						
14110 - 4	ما م ماه م ماه		unding diseases	(110)		a da da a la a
AUC <sub>0-t</sub> = Area u	inder the pla	sma-concen	tration-time (	curve (AUC) I	from time zer	o to the las
quantifiable con	centrations					
$2\Delta I I C = \Delta I I C f$	rom time zero	to infinity				
AUOULint - AUUI	10111 01116 2010	, co mininey				

\* n=21 MICROBIOLOGY: Florfericol 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. Florfericol is generally considered a bacteriostalic durp, but exhibits bacterioida activity against certain bacterial species. In vitro studies demonstrate that florfericol is active against the BRD pathogens M. haemolytica, P. multooda, and M. Somri, and M. Movis that florfericol exhibits bactericidal activity against strains of M. haemolytica and H. sommi.

activity against stains of M. haemolytica and H. sommi. The minimum inhibitory concentrations (MICs) of fiorfenicol were determined for non-mycoplasmal BOI isolates obtained from calves enrolled in BRD field studies in the U.S. n 2006 using methods recommended by the Clinical and Laboratory Standards Institute M31-A2. MICs for M. box's loates were determined by an accepted method using Hayflick Stoth with Alamar Blue (HBAN) medium under appropriate control. Isolates were obtained from er-teratment faals webs from all calves enrolled at all four sites, post-teratment nasal swabs rom treatment failures in the RESFLOR GOLD and saline control treatment groups at three sites, and lung issue 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-

Indicated pathogens	Year of isolation	Number of isolates	MIC <sub>50</sub> ** (µg/mL)	MIC <sub>90</sub> ** (µg/mL)	MIC range (µg/mL)
Mannheimia haemolytica	2006	183	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 0.25
Mycoplasma bovis	2006	60	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, respective EFFECTIVENESS: In a multi-site field study, calves with naturally occurring BRD were treated with RSFLOR GOLD\*, Multior Gold\* (NADA 141-265), or saline. A treatment success was defined as a call 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 8PD for the RESELRG GOLD<sup>®</sup> treatment group (68.4%) was statistically significantly greater (p = 0.0255) compared to the saline control treatment group (4.2%), RESELRG ROLD<sup>®</sup> was non-inferior to Nuffor Cold<sup>®</sup> for the treatment of RPD, with a one-sided 95% lower confidence bound for the difference between the two treatments equal to -13.2%.

sided 5% lower confidence bound for the difference between the two treatments equal to -1.32%. In the same subuly the change in recalst temperature from york-treatment to six hours post-reatment was evaluated to determine the effectiveness of RESFLOR GOLD<sup>6</sup> for the control of BRD-associated pryrexia. The proportion of calkes whose rectal temperatures decreased by 2.0 °F from per-treatment to six hours post-treatment was statistically significantly greater (p = 0.0019) in the RESFLOR GOLD<sup>6</sup> treatment group compared to the siline control treatment was statistically significantly greater in the RESFLOR GOLD, reatment group compared to the value of silication silication of the temperature from per-treatment to so thrours post-treatment was statistically significantly greater in the RESFLOR GOLD, creater with value of solid and silice control treatment groups (p = 0.0031 and 0.0002, espectively). The effectiveness of RESFLOR GOLD<sup>6</sup> for the treatment of BRD associated with *Mycoplasma* box's was demonstrated by examining the *M. Jovis* data from cattle enrolled in the BRD treatment study described above. There were numerically more treatment sourcesses (6 of Section 2.2%) in RESFLOR GOLD<sup>6</sup>-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 does 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 X, 3X, and 5X groups. Injection size wellings 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 in the subcutaneous and underlying muscle tissue.

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

Intervet Inc. a subsidiary of Merck & Co. Summit, NJ 0790

Rev. 7/12



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

Made in Germany

© 2009, Intervet Inc. All rights reserved.

NUFLOR<sup>®</sup> (florfenical) Approved by FDA under NADA # 141-063

iectable Solution

300 mg/mL For intramuscular and 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 proce for yeal. CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinanan. DESCRIPTION: NUFLOR Injectable Solution is a solution of the synthetic antibiotic florfenicol. Each milliliter of sterile NUFLOR Injectable Solution contains 300 mg of florfenicol. Each milliliter of sterile NUFLOR Injectable Solution is a solution contains 300 mg of florfenicol. So mg N-methyl-2-pyrolidome (NMP). 150 mg propylene glycol, and polyethylene glycol, son. The chemical name for florfenicol is 22-Dichloro-NI-fl (flucomethyl)-2-hydraxy-2-14-(methylsulfonyl)dhenyl/fethyl] acetamide. INDICATIONE: NUFLOR Injectable Solution is indicated for treatment of bovine respiratory disease (BRD) associated with Mannheimia haemohytica. Pasteurella multocida, and Histophilus zomi, and for the treatment of bovine interdigital plengtom (for tor, acute interdigital necrobacillosis, infectious pododermatifis) 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 haemohytica. Pasteurella multochaet and Histophilus sonni. DOSAGE AND ADMINISTERATION: For treatment of bovine respiratory disease (BRD) and

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 subsysteme in the state 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 (Pounds)	IM NUFLOR DOSAGE 3.0 mL/100 lb Body Weight (mL)	SC NUFLOR DOSAGE 6.0 mL/100 lb Body Weight (mL)	Recommended Injection Location	
100	3.0	6.0		
200	6.0	12.0	A DO	
300	9.0	18.0		
400	12.0	24.0		
500	15.0	30.0	/ ۲	
600	18.0	36.0	l D	
700	21.0	42.0		
800	24.0	48.0		
900	27.0	54.0	Do not inject more that 10 ml per injection sit	
1000	30.0	60.0	To me por injuotion of	

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 ISER SAFETY WARNINGS: NOT FOR HUMAN USE, KEEP OUT OF REACH OF CHILDREN

USER SAFE I Y 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 scap and water. Remove contaminated clothing. Consult a physician i firritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. Reproductive and developmental toxicities have been reported in laboratory animals following high, repeated exposures to *N*-methyl-2-pyrolidone (NMP). Pregnant women should wear gloves and exercise caution or avoid handling this product. The Safety Data Sheet (SDS) contains more detailed occupational safety information.

CONTACT INFORMATION: For customer service, adverse effects reporting and/or a copy of the SDS, call 1-800-211-3573. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov

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

RESIDUE WARNINGS: Animals intended for human consumption must not be slauphtered within 28 days of the last intramuscular treatment. Animals intended for human consumption must not be slauphtered 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 cattles born to these cows. A ithdrawal period has not been established in pre-ruminating calves. Do not se in calves to he processed for yeal.

ADVERSE REACTIONS: Inappetence, decreased water consumption, or diarrhea may occu

CLINICAL PHARMACOLOGY: The pharmacokinetic disposition of NUELOR Injectable Curroter Proceedings of the provided of the pr 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 <sub>max</sub> (µg/mL)	3.07*	1.43 - 5.60		
t <sub>max</sub> (hr)	3.33	0.75-8.00		
T <sub>1/2</sub> (hr)	18.3**	8.30 - 44.0		
AUC (µg•min/mL)	4242	3200-6250		
Bioavailability (%)	78.5	59.3 - 106		
Vd <sub>ss</sub> (L/kg)***	0.77	0.68 - 0.85		
Cl <sub>t</sub> (mL/min/kg)***	3.75	3.17 - 4.31		
* harmonic mean ** mean value	Cmax Maximum serum concentration Tmax Time at which Cmax is observed			

T12 Biological half-life AUC Area under the curve Vd<sub>ss</sub> Volume of distribution at steady state Cl<sub>t</sub> 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 flor-fenicol was 12.7%, 13.2%, and 18.3% at serum concentrations of 0.5, 3.0, and 16.0 µg/mL, respectively. MICROBIOLOGY: Florienicol is a synthetic, broad-spectrum antibiotic active against many Gram negative and Gram-positive bacteria isolated from domestic animas. It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis. Florienicol is generally considered a bacteriostatic drug, but exhibits bactericidal activity against certain

#### TAKE TIME \*Umax = Minimum plasma concerne autor 4T<sub>max</sub> = Time at which Cmax was observed 5T<sub>w</sub> = Terminal elimination half-life \*MRT<sub>0-Inf</sub> = Mean residence time from time zero to infinity **OBSERVE LABEL** DIRECTIONS

bacterial species. In vitro studies demonstrate that florfenicol is active against the bovine social applices in mice social social constraints and the social social application of social social

'he minimum inhibitory concentrations (MICs) of florfenicol for BRD organisms were letermined using isolates obtained from natural infections from 1990 to 1993. The MICs retretigital phlegmon organisms were determined using isolates obtained from natura fections from 1973 to 1997 (Table 2).

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

dicated Pathogens	Year of Isolation	Isolate Numbers	MIC <sub>50</sub> ** (µg/mL)	MIC <sub>90</sub> ** (µg/mL)
Mannheimia haemolytica	1990 to 1993	398	0.5	1
steurella 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

n the in vitro susceptibility data and clinical effectiveness is unknown mpass 50% and 90% of the most susceptible isolates, respectively The correlation betwe

INIMAL SAFETY: A 10X safety study was conducted in feeder calves. Two intramuscula iections of 200 mg/kg were administered at a 48-hour interval. The calves were monitored at a 48-hour interval. jections of 200 mg/kg were administered at a 48-hour intervat. Ine carves were movimues r 14 days after the second dose. Marked anorexia, decreased water consumption, decrease dy weight, and increased serum enzymes were observed following dose administration rese effects resolved by the end of the study.

I nese effects resolved by the end of the study. A 11, 32, and 52, 02, 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 does group. Decreases let ead and water consumption, body weight, urine pH, and increased serum enzymes, were observed in the 3X and 5X does groups. Degression, soft stod consistency, and dehyrdation were also observed in some animals (most fre-quently at the 3X and 5X does 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 tran-sient 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.

Protect from light when not in use. Use within 30 days of first puncture. For the 100mL vials, puncture the stopper a maximum of 3 times. For the 250mL and 500mL vials, puncture the stopper a maximum of 71 times.

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

Forfenicol (active ingred.) made in China. Formulated in G

#### ZUPREVO<sup>®</sup>(tildipirosin)

Injectable Solution for Cattle Antimicrobial Drug

Rev. 01/2022

180 ma of tildipi

Figure 1

Bacteroid nelaninoger

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

DESCRIPTION: Zuprevo<sup>®</sup> 18% contains 180 mg of tildipirosin as the free base, 82.5 mg citric cid monohydrate and 400 mg propylene glycol, and water qs with citric acid monohydrate ded to adjust pH. CHEMICAL NOMENCLATURE AND STRUCTURE: Tildipirosin is the nonproprietary na

for (TIE, T35)- (48, SS, 65, 78, 98, TSK, 168, 1-6(4-Dimethylamino-3,5-dihydroxy-6-me tetrahydro-pyran-2-yloxy)- 16-ethyl-4-hydroxy-5,9,13-trimethyl-7-z)erperdin-tetrahyl-Ts-piperdin-1-ylmethyl-xoaxyclohexadea-11,13-dimez, 21,0-dione. The empi formula is C41H71N308. The chemical structure of tildipirosin is shown below.



INDICATIONS: Zuprevo<sup>®</sup> 18% is indicated for the treatment of bovine respiratory disease (BRD) associated with Manpheimia baemolytica. Pasteurella multocida, and Histophilus sond associated with Manihamina intermotytical, associated and initiatious, and mouthing associated with Manihamina intermotyticas sommi 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 Mannheimina haemolytica, Pasteurella multicola, and Histophilus sommi.

DOSAGE AND ADMINISTRATION: Inject subcutaneously as a single dose in the neck at a desage of A 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) Inje 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:

<ul> <li>Cauce as inguitation to developing onco-called at ingli task of developing both typical experience one more of the following risk factors:</li> <li>Commingling from multiple sale barnshources</li> <li>Expended transport times and shrink         <ul> <li>Expended transport times and shrink</li> <li>Disourate to well could weather conditions or windle temperature swings</li> <li>Stressful arrival processing procedures (such as castration, dehorning, or branding)</li> <li>Resent wearing and poor vaccination history</li> </ul> </li> </ul>				
Vial size (mL)	Number of punctures tested in the in-use study			
50	50 8			
100	8			
250	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 SYNINGES 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.ov/AnimalVeterinary/SafetVeleIth.

DO NOT USE ZUPREVO®18% IN SWINE. Fatal adverse events have been reported

NOT FOR USE IN CHICKENS OR TURKEYS.



PRECAUTIONS: The effects of 7uprevo®18% on hovine reproductive performance 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. Suboutaneous injection may result in local tissue reactions which persist beyond the slaughter withdrawal period. This may result in trim loss of edible tissue at slaughte

CLINICAL PHARMACOLOGY: Similar to other macrolides, tildipirosin inhibits essentia bacterial protein biosynthesis with selective binding to ribosomal subunits in a bacterio and time-dependent manner. Tildipirosin may be bactericidal against certain isolat Mannhaimis haamolutica and Pasteuralla multicorida

The following plasma pharmacokinetic (PK) properties of tildipirosin have been observed following a subcutaneous injection at a dose of 4 mg/kg body weight 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 <sub>max</sub> (ng/mL)	767*	284
T <sub>max</sub> (hr)	0.75*	0.43
AUC <sub>0-last</sub> (hr·ng/mL)	21017**	3499
AUC <sub>0-inf</sub> (hr·ng/mL)	24934**	3508
t <sub>1/2</sub> (hr)	210**	53

Value based on all 14 animals

\*\* Value based on 8 animals that were slaughtered at 504 hr post-treatment.

....: maximum observed plasma concen T<sub>max</sub>: Time at which Cmax was observed

 $^{\rm MIC}_{\rm D_{bast}}$ . 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

 $\mathsf{AUC}_{\text{0-inf}}$  AUC estimated from time zero to time infinity

tup: 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." This is shown for tildipriors 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: 
 REFERENCE:
 Column KJ, et al. Pharmacokinetics of florfenicol following intravenous and intramuscular does to cattle. J Vet Pharmacol Therap. 1994;17:255-258.
 calves, and compared to the concentrations in plasma observed in these same animals.

 Copyright@ 1996, 2022 Intervet Inc., a subsidiary of Merck & Co. Inc., Madison, NJ 07940. All
 Table 3. Bronchial fluid-to-plasma ratio of tildipriosi in non-anesthetized cattle following a subcuraneous injection at a dose of mg/kg body weight in the neck.

Time (hours)	Bronchial fluid (BF) concentration (ng/g)		Plasma (P) concentration (ng/mL)		BF/P Ratio
	Average	SD	Average	SD	1
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.

Nightingale, C.H. (1997) Pharmacokinetics and pharmacodynamics of newer macrolide: The Pediatric Infectious Disease Journal, 16, 438-443.

MICROBIOLOGY: Tildipirosin has shown in vitro and in vivo antibacterial activity against the bacteria Mannheimia haemolytica, Pasteurella multocida, and Histophilus somni, three pathogens associated with bovine respiratory disease (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.

Clinical and Laboratory Standards Institute (LSI) and are shown in Table 4. The MICs of tidpirosin were determined for isolates of Mannheimia haemolytica, Pasteurella multocida, and Histophilus somni obtained from two BRD field studies. In both studies, tested isolates of M. haemolytica and P. multocida were obtained from nasopharyngeal swebs taken prior to treatment from all study animals. Tested isolates of H. somni were obtained from nasopharyngeal swebs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from nasopharyngeal swabs taken prior to treatment from all study animals and from the prior to the prior to treatment from all study animals and from the prior to the prior

Table 4. Tildipirosin minimum inhibitory concentration (MIC) values\* of indicated pathogens isolated from BRD field studies in the 11%

Indicated Pathogens	Year of Isolation	Study	Number of Isolates	MIC <sub>50</sub> ** (µg/mL)	MIC <sub>90</sub> ** (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 RBN 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 success was opened as a call 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 (b = 0.003) for the tildiprioriinteated group (229/300, 76%) compared to the salme-treated control group (96/200, 32%). There were no BRD-related deaths in the tildiprioriin-treated group, compared to a 7% (21/300) SRD-related mortality rate in the salme-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

ZUPREVO con't next page..

#### 7LIPREVO con't

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 socing 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 = 0.0000)11 for the tildipricesin-treated group (050/366, 79%) compared to the saline-treated group (1977/387, 51%). There were three BRD-related deaths during the study (one tildiprices in-treated call and two saline treated calves).

study (one tudiprosin-treated call and two saline treated calves). **ANIMAL SAFET:** A target animal safety study was conducted using Zuprevo\*18% administered in 5-month-old cattle as three subcutaneous doese of 4, 12, or 20 mg (g BW given 7 days apart (1X, 3X, and 5X the labeled does), hinitias remained clinically healthy during the study at the labeled does, 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 doee.

Aseparate injection site tolerance study was conducted using Zuprevo<sup>®</sup> 18% in 5-to 9-month old cattle administered as a single subcutaneous injection of 10 mL Injection site swellin and inflammation, initially severe in some animals, was observed that persisted to the last da 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,

U. S. Patent: 6.514.946

Approved by FDA under NADA # 141-334

- Use Only as Directed
- Copyright © 2011, 2019 Intervet Inc., a subsidiary of Merck & Co.
- All rights reserved. Rev. 02/2019

Tildipirosin (active ingred.) made in Switzerland. Formulated in Germany. Distributed by: Intervet Inc d/b/a Merck Animal Health, Madison, NJ 07940

#### **BANAMINE<sup>®</sup> TRANSDERMAL**

NADA #141-450, Approved by FDA

(flunixin transdermal solution) Pour-On for Beef and Dairy Cattle

#### 50 mg/mL

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 bed cabes, dairy cahes, and veal cabes, and veal cabes. 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 mg propylene glycol monocaprvlate NF gs.

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.

**DOSAGE AND ADMINISTRATION:** Apply only once at a dose of 3.3 mg flunixin per kg body weight (1 5 mg/lb; 3 m per 100 lb) tonically in a parrow strin along the dorsal midling from Weight (1.5 high), offic per too high optically in a history and painting the obtaining the other the withers to the tailhead. A bound all doses up to the nearest weight increment on the dosing chamber. Do not treat cattle if the hide is wet or may get wet in the six hours after dosing because effectiveness has not been evaluated under wet hide conditions.

stration and Overfill Reduction Instructions a few times to be ackage before dosing animals.



Pour the measured volume or dorsal midline from withers to head. Application to a small a should be avoided.

A small amount of liquid will remain on the walls of the chamber, but the chamber is calibrated to account for this. OVERFILL REDUCTION INSTRUCTIONS:





Tilt the bottle to allow an air pocket to form at the beginning of the transfer tube inside the

Step 3 Transfer Tube





53

CONTRAINDICATIONS: NSAIDs inhibit production of prostaglandins which are important n signaling the initiation of parturition. The use of flunixin can delay parturition and noolong 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 meglumine USER SAFETY WARNINGS: Not for use in humans. Keep out of reach of children. Flunixin

transfermal solution is a potent non-steroidal anti-inflammatory drug (NSAID), and ingestion may cause gastrointestinal irritation and bleeding, kidney, and central nervous system effects.

If this product has been shown to cause severe and potentially irreversible eye damage conjunctivitis, inits, and corneal opacity) and irritation to skin in laboratory animals. Users hould wear suitable eye protection (face shields, safery glasses, or oggles) to prevent eye contact; and chemical resistant gloves and appropriate clothing (such as iong-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 herore 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 mucos

RESIDUE WARNINGS: Cattle must not be slauphtered 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 heries. Not for use in suckling beef calves, dairy calves, and veal calves. A withdrawal period has not been with the such that the such and the such as the suc beef calves, dairy calves, and veal calves. A withorawa established for this product in pre-ruminating calves.

Pestablished for this product in pre-ruminating cakes.
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 diureit therapy, or those with renal, cardiovascula, and/ or hepatic dysfunction. Banamine transdermal should be used with caution in animals with suspected pre-existing gastric evolutions. Concurrent administration of other NSAIDs, corticosteroids, or potential frequential 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 (MSAIDs are known to have the estrous cycle. NSAIDs are known to have there estrol effect. The used ONSAIDs in the immediate post-partum period may interfere with uterine involution and expulsion of fetal membranes. Cows should be emolited carefully for placental retention and metritis if Banamine

yows should be monitored carefully for placental retention and metritis if Banamine ransdermal 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

CINICL PHARMACOLOGY: Flunixin meglumine is a nonsteroidal, anti-inflammatory drug, It is a weak acid (pka-5,82) which exhibits a high degree of plasma protein binding (approximately 99%)- However, free (unbound) drug appears to readily partition into body tissues (Vss predictions range from 297 to 782 mL/kg)<sup>2,4</sup> In cattle, elimination occurs minarily through bilisroy exercisi

Itssues (vs.p. preductions larger monitor). Flunchin persists in inflammatory tissues? and is associated with anti-inflammatory properties which extend well beyond the period associated with detectable plasma drug concentrations.<sup>44</sup> 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. Pharmacokinetic properties of flunxin transchermal solution in cattle administered at a dose of 2.5 mg/kg, are summarized in Table 1, comparing results between animals that were allowed to self- or allo-lick had lower rate and extent of absorption when compared to the animals prevented from licking. However, on dose adjustment is needed to account for the animals prevented from licking. However, on dose adjustment is needed to account for the animals prevented from licking. However, on dose adjustment is needed to account for the animals mater allowed to lick. **Table 1.** Average (+/ standard deviation [SD]) PK parameters after a single administration of flunxin transdermal solution at a dose of 2.5 mg/kg in cattle that were eilowed to lick or prevented from lick.

PK parameter	Non-licking		Licking	
	Mean	± SD	Mean	± SD
C <sub>max</sub> (ng/mL)	1496	769	N/A	N/A
Concentration at 2 h*	1282	533	1072	353
T <sub>max</sub> (h)	1.29	0.464	N/A	N/A
AUC <sub>2-last</sub> (ng*h/mL)	7499	2131	6827	4672
T <sub>1/2</sub> (h)	8	2	9	6

\* First blood level in the licking group was taken at 2 hours post-dose. First blood sample in non-licking group was taken at 0.25 hours post-dose.

Cmax: Maximum observed plasma concentration x: Time at which C<sub>max</sub> was observed

AUC<sub>2-last</sub>: Area under the plasma concentration versus time curve measured between 2 hours and the time of the last supertificial

T<sub>1/2</sub>: Terminal elimination half-life Fig.2 reminate immachance and a solution in cattle is dependent on environmental temperature. The effect of temperature on flunxin absorption was tested in temperatures ranging from 15.3 to 20.1 °F (average low in the coldest study) to 80 to 100 °F (average high in the varmest study). Flunxin concentrations were consistently lower when the pour-on product was administered in a cold (temperature) and than hot (temperature) environment. However, the clinical effectiveness was demonstrated over the range of environmental conditions expected under field conditions. No dose adjustments are necessary due to environmental temperature.

#### BANAMINE® Intervet/Merck Animal Healt

NADA 141-450, Approved by FDA

Use Only as Directed

nts reserved.

e in Germany

5/2017

196764 R1

CPN: 1047536.0

ved by FDA under NADA # 101-479 n meglumine injection)

50 ma/mL 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.

Application site reactions, including dandruff/skin flakes, hair damage (thin, broken, brittle hair

Appreciation site reactions, including dandruin/skinnakes, nan danage (nin, broken, ontide nan and skin thickening were observed in effectiveness and/or supportive studies. The applicatio site reactions were first observed around three to seven days post-dosing and lasted for about 14 days. These reactions were cosmetic in nature and generally resolved without treatment.

of BANANINE (flunixin meglumine injection) in cattle, NADA 101–479. EFFECTVENESS: Pharmacolinetics studies established that the absorption of flunixin administered transfermally to cattle is highly dependent on environmental temperature. Therefore the effectiveness of flunixin transfermal solution for the control of prexia associated with bovine respiratory disease was demonstrated under a range of environmental temperatures in two studies: a field study conducted at four geographic locations (California, Kansas, Nebraka, and Toxas) under moderate environmental temperatures (average timperatures ranged from 2-17 to 27 to en renolment days) and a field study conducted to 2 studies in 24 field studies (average temperatures ranged from 2-16 roz). To 4 ron environmental from 2-16 roz) for en environment average temperatures ranged from 2-16 roz) for en environment average temperatures around and the prevented from licking.

In both studies, cattle exhibiting clinical signs of BRD and having a rectal temperature of at least 104.5 Twere enrolled. A total of 235 cattle in the multi-location field study and 50 cattle at the single site field study were administered either flunixin transfermal solution (3.3 mg/kg BW) or an equivalent volume of dyed saline as a pour-on once on Dy 0. Six hours after treatment, rectal temperatures were measured. The treatment success rate of the flunixin transfermal solution-treated group was compared to the treatment success rate in the dyed saline-treated group. A treatment success was defined as a drop in rectal temperature of a 2 °F in an individual animal. In the multi-location study, the treatment solution-treated group (7) true, 53.3% (ompared to the dyed saline-treated control group (7) T15, 6.1%). In the single site study, the treatment success rate was significantly different (b = 0.0002) and higher for the flunixin transfermal solution (p = 0.0002) and higher for the flunixin transfermal solution fracted group (19/25, 76%) compared to the dyed saline-treated control group (4/25, 16%).

compared to use upper samme-treated control group (4/25, 19%). The effectiveness of flunixin transformal solution for the control of pain associated with foot to in beef and dairy cattle was demonstrated under a range of environmental temperatures in two studies an induced infection model study conducted in Nebraska with temperatures ranging from 61 °F to 65 °F on the day of enrollment and treatment; and an induced infection model study conducted in Kansas with temperatures ranging from 31 °F to 53 °F on the day of enrollment and treatment. In both studies, cattle from both treatment groups were commingled in pens and were not prevented from licking.

groups were commingled in pens and were not prevented from licking. In each study cattle were challengend by subcutancew sinjection of a culture of *Fusobacterium necophoum* into the interdigital space of the right front foot using a method that was validated to induce pain representitive of foot rot. Cattle were enrolled when they demonstrated signs of pain associated with foot rot based on lameness, interdigital lesion, and interdigital swelling criteria. Pressure mat gait parameters maximum total force kg/j and contact area (cm2) were also measured at enrollment. A total of 30 cattle at each site were

contact area (cm2) were also measured at enrollment. A total of 30 cattle at each site were administered either flunixin transdermal solution (3.3 mg/kg BW) or an equivalent volumu of dyed saline as a pour-on once on Day 0. Six hours after treatment, lameness scores and pressure mat gait parameters maximum total force and contact area were measured.

pressure mat gain parameters maximum total torce and contact area were measured. Effectiveness was determined independently at each site based on treatment success rates at six hours after treatment; and the change in maximum total force and contact area between enrollment and six hours after treatment. A treatment success was defined as a decrease in lameness score by 2 (scale 1 to 5, with enrollment to aimals with hameness score 2 3) from the enrollment lameness score. The treatment success rate of the flunixin transfermal solution-treated group was compared to the treatment success rate in the dyed saline-treated group at both sites.

Changes in biometric galt parameters were also compared between the treatment groups. In the Nebrask study, the treatment success rate was significantly different and higher for the fluxium transdermal solution-treated group (15/15, 10%) compared to the dyed saine-treated group (1/15, 6.57%), and the mean change in maximum total force and mean change in contact area were statistically significantly different [0 - 0.0001] and higher in the fluxium transdermal solution-treated group (4.16, kgr] and 1.57.6 cm.2) compared to the dyed saline-treated control group (4.14, kgr] and -2.70 cm.2). In the Kansas study, the treatment success rate was significantly different [0 - 0.0007] and higher for the fluxion transdermal solution-treated group (14/15, 93.3%) compared to the dyed saline-treated group (15, 53.33%), and the mean change in maximum total force and mean change in contact area were statistically significantly different (p - 0.0002 and p-0.0001, 16.32 kgr] and thigher in the fluxinis transderma is olution-treated group (3.42 kgr] and 16.38 cm.2) compared to the dyed saline-treated control group (-0.54 kgr] and -0.96 cm.2). CONTACT INFORMATIONE For the chronical assistance on to remort a superied adverse drug

CONTACT INFORMATION: For technical assistance or to report a suspected adverse drug experience, call: 1-800-219-9286

For customer service or to request a Safety Data Sheet (SDS), call: 1-800-211-3573.

For additional Banamine Transdermal pour-on information go to www.BanamineTD.com For additional information about adverse drug experience reporting for animal drugs, contac FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

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.

STORAGE INFORMATION: Store at or below 30°C (86°F). Use within 6 months of first opening.

For Patent information: http://www.merck.com/product/patent/home.html

Distributed by: Intervet Inc. d/b/a Merck Animal Health, Madison, NJ 07940

Copyright © 2017, Intervet Inc., a subsidiary of Merck & Co.

etric gait parameters were also compared between the treatment groups.

- ....service consumers in nature and up generally resolved without treatment. macokinetic evaluation demonstrated that the systemic exposure of flunixin is ly lower when administered transdermally at a dose of 3.3 mg flunixin/kg BW that dministered intravenously at a dose of 2.2 mg flunixin/kg BW, therefore, female crive safety is supported by reproductive safety studies conducted for the approval MINE (flunixin meglumine injection) in cattle, NADA 101-479.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. DESCRIPTION: Each milliter of BANAMINE (fluxion meglumine injection) constains 50 mg fluxibin (equivalent to 83 mg fluxibin meglumine), 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 preservitive, hydrochloric acid, water for injection ops. PHARMACOLOGY: Fluxibin meglumine is a potent, non-narotic, nonsteroidal, analgesis agent with anti-inflammatory and antipyetic activity. It is significantly more potent than pentazone, meperidine, and codeine as an analgesic in the rat yeast paw test.

permaschane, inegrenune, and usualene as all ratifigiest in the fart 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 all Bhours postingction.

Bhourspostinjörction. Cattle: Flunixin meglumine is a weak acid (pKa=5.82)\* which exhibits a high degree of plasma protein binding (approximately 99%).<sup>2</sup> However, free (unbound) drug appears to readily partition into body tissues (W<sub>2</sub> predictions range from 29 To 782 mL/kg<sup>2-3</sup> Total body water sapproximately equal to 570 mL/kg)<sup>1</sup> In cattle, elimination occurs primarily (through bilary excetion:<sup>2</sup> This may, at least in part, explain the presence of multiple peaks in the blood concentration/time profile following V administration.<sup>2</sup> In healthy cattle, total body clearance has been reported to range from 90 to 151 mL/kg/hr<sup>2-3</sup> In healthy cattle, total body clearance has been reported to range from 90 to 151 mL/kg/hr<sup>2-3</sup> U<sub>2</sub>. This discrepancy appears to bartibutable to extended drug elimination from a deep compartment.<sup>3</sup> The terminal half-life has been shown to vary from 3.14 to 8.12 hours.<sup>2-3</sup> Unbins excited in information is imposed and incompland multiple means the mean distingtion management of the site of the advection of the site of

ory tissues<sup>9</sup> and is associated with anti-in period associated with detectable plasma

which extend well beyond the period associated with detectable plasma drug concentration These observations account for the counterclockwise hysteresis associated with fluni

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: RANAMINE (flunixin meglumine injection) 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. Horse & Cattle Deworme

associated with bovine respiratory disease, endotoxemia and acute bovine mastitis BANAMINE is also indicated for the control of inflammation in endotoxemia. DOSE AND ADMINISTRATION: USE WITHIN ADMINISTRATION IE AND ADMINISTRATION: USE WITHIN 20 ADMINISTRATION: USE WITHIN 20 ADMINISTRATION: USE WITHIN 20 ADMINISTRATION: USE WITHIN USING A DRAW-OFF SPIKE OR NEEDLE WITH GORE DIAMETEE LARGEE THAN 18 GAUGE, DISCARD ANY PRODUCT REMAINING IN THE VIAL IMMEDIATELY AFTER USE.

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.

Dependence out of stretch and refrain a duration of pairs associated with equine colic is 0.5 mg per pound of body weight. Intravenous administration is recommended for prompt relief. Clinical studies show pairs is alleviated in less than 15 minutes in many cases. Treatment may be peeted when signs of colic recur. During clinical studies approximately 10% of the horses equired one or two additional treatments. The cause of colic should be determined and treated with oncomitant theraw.

and endotoxemia and control of inflammation in endotoxemia, is 1.1 to 2.2 mg/kg (0.5 to 1 mg) b; 1 to 2 m Lper 100 lbs) of body weight given by solve 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 dai/ dose should not exceed 2.2 mg/kg (1.0 mg/lb) of body weight. Avoid ranid 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 ody weight given once by intravenous administration.

CONTRAINDLATIONS: Hows: These are in known contraindications to this drug when used as directed. Intra-aterial injection should be avoided. Horses inadvertently injected intra-arterially can show adverse reactions: Signs can be abata, incoordination, hyper-entilation, hysteria, and muscle weakness. Signs are itaraisent and disappear without antibiotal medication within a few minutes. Do not use in horses showing hypersensitivity to fluxionine.

Cattle: MSADs inhibit production of prostgalandism 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 (flunixin meglumine injection) 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.



lorse: The effect of BANAMINE (flunixin meglumine injection) on pregnancy has not been letermined. Studies to determine activity of BANAMINE when administered concomitantly with other drugs have not been conducted. Drug compatibility should be monitored closely in patients requiring adjunctive therapy.

patents requiring adjunctive timapy. Cattle: Do not use in bulls intended for breeding, as reproductive effects of BANAMINE (flunixin meglumine injection) 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 estrus cycle. NSAIDs are known to have the potential to delay parturition through pnase of the estrous cycle. NSAIUS are known to nave the potential to dealy partuntion thr a tocolytic effect. The use of NSAIDs in the immediate post-partum period may interfere therine involution and expulsion of fetal membranes. Cows should be monitored careful placental retention and metritis if BANAMINE is used within 24 hours after parturition.

lorse: A 3-fold intramuscular dose of 1.5 mg/lb of body weight daily for 10 consecutive days

No changes were observed in hematology, serum chemistry, or urinalysis values. Intravenous dosages of 0.5 mg/b daily for 15 days, 1.5 mg/b daily for 10 days, and 2.5 mg/b daily for 5 days produced no changes in blood or urine parameters. No injection site initiation observed following intranuscular injection of the 0.5 mg/b recommended dose. Some iritation was observed following a 5-old dose administered intranuscularly.

Cattle: No flunicin-related changes (adverse reactions) were noted in cattle administered a 1X (22, mg/kg; 1:0 mg/b) dose for 9 days (three times the maximum clinical duration), Minimal toxicity memfested tails 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. Decontinue use the Hematuria or feasiblood are observed. Distributed by:

uscurntule use in rematuria or tecal 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 (flunxin meglumine injection). 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 (flunixin meglumine injection), 50 mg/mL, is available in 100-mL (NDC 0061-0851-03), and 250-mL (NDC 0061-0851-04) multi-dose vials. Store at or below 25°C (77°F) Do not Freeze. See the in-use directions provided in the DOSE CPN: 1047343.3
AND ADMINISTRATION continu

**BO-SE°** 

AND ADMINISTRATION section. **REFERENCES:** Voltansson M, Anler EL. Gas chromatographic analysis of flunixin in equine urine after extractive methylation. *Othomatogr.* 1988;427:55-66. Odensvik K, Johansson M. High-performance liquid chromatography method for determination of flunixin in bovine plasma and pharmacolinetics after single and repeated doese of the drug. *Am J Vet Res.* 1995;56:6439–4307. "Anderson KL, NetF-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. "Odensvik K, Pharmacokinetics of flunixin and its effect on prostaglandin F<sub>20</sub> metabolite concentrations after oral and intravenous administration in heifers. *J Vet Pharmacol Ther.* 1004;18:74.2760

1995:18:254-259

Hardee GE, Smith JA, Harris SJ. Pharmacokinetics of flunixin meglumine in the cow. Res Vet 67: 1985;39:110-112.

Sci. 1985;39:110-112. "Ruckebusch: Whaneuf JP, Dunlop R. Physiology of Small and Large Animals. Chapter 2: "Body Fluid Compartments" Philadelphia, Pa: BC, Decker, 1991;8:18. "Kopcha M, Ah JA & Experimental uses of fluxinism englumine and phenylbutazone in food-producing animals. *JAm Het Med* Assoc. 1999;19:445-49. "Wagner JG. Significance of ratios of different volumes of distribution in pharmacokinetics. *Biopharm & Drug Dispos.* 1963;4:263-270.

 Grand Construction (Construction)
 Grand Construction (Construction)
 Grand Construction (Construction)
 Construction (Construction)
 Construction (Construction)
 Construction (Construction)
 Construction
 Construction Ver/Sci 1994;37:347-349. "Wandoni MF, Cunningham FM, Lees P. Determination of pharmacokinetics and pharmacodynamics of flunkini in calves by use of pharmacokinetic/pharmacodynamic modeling. *Am J Ver Res*. 1995;65:766-794. Distributed by: Intervet Inc d/b/a Merck Animal Health, Madison, NJ 07940

Copyright@2011-2021 Intervet Inc., a subsidiary of Merck and Co., Inc. All rights reserved.

Formulated in Germany by: Vet Pharma Eriesovthe GmbH

399673 R1 Rev. 11/2021

CPN: 1047018.8





Hardee GE, Smith JA, Harris SJ. Pharmacokinetics of flunixin meglumine in the cow. Res Vet Sci. 1985; 39:110-112. Lees P, Higgins AJ. Flunixin inhibits prostaglandin E2 production in equine inflammation. *Res Vet Sci.* 1984: 37:347-349.

Takes Vet 3C: 1984; 37:347:349.
TARGET ANIMAL BARETY: In a target animal safety study in 32 six-month old bed catter to the safe of the formales. In this international transformal solution was administered topically at 3.3, 9.9, and 16.5 mg/kg body weight (1X, 3X, and 5X the labeled dose) on Days 1, 2, and 3 (3X the labeled dose) and 16.5 mg/kg body weight (1X, 3X, and 5X the labeled dose) on Days 1, 2, and 3 (3X the labeled dose) and 16.5 mg/kg body weight (1X, 3X, and 5X the labeled dose) on Days 1, 2, and 3 (3X the labeled dose) and 16.5 mg/kg body weight (1X, 3X, and 5X the labeled dose) on Days 1, 2, and 3 (3X the labeled dose) and 16.5 mg/kg body weight (1X, 3X, and 5X the labeled dose) and 18.5 mg/kg body and 19.5 mg/kg

CONTRAINDICATIONS:

EXAMPLES:

PRECAUTIONS: As a class, cyclo-oxygenaes 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 (flumixin meglumine injection) with other anti-inflammatory drugs, such as the total dividual patient in the sense of the sense in meglumine injection) with other anti-inflamma osteroids, should be avoided or closely monitored. ther NSAIDs and cortic

### PANACUR®

#### Suspension 10% (100 mg/mL)

WITHDRAWAL PERIODS AND RESIDUE WARNINGS: Milk taken from TUTURAWAL PENDUS AND RESIDUE WARNINGS. Milk taken from cows during treatment and for 48 hours after the last treatment must not be used for human consumption. Cattle must not be slauphtered for human consumption within 8 days following last treatment with this drug product. Not for use in beef calves less than 2 months of age, dairy calves, and veal calves. A withdrawal peniod has not been established for this product in pre-ruminating calves.

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

CAUTION: Fourier terms reasonance INDICATIONS AND DOSAGE: Horses - 23 mg/hg/s mg/kg/s for the treatment and control of large strongyles (Cyrathostomum spp., Cyticocyclus spp., Cyticostephanus spp., Cyticodontophorus spp.), and Istrongyles (Cyrathostomum spp., Cyticocyclus spp., Cyticostephanus spp., Cyticodontophorus spp.), and pinwoms (Oxyuris equi). 4.6 mg/b (10 mg/kg): for the treatment and control of ascarids (Parascaria

sporting. Seef and Dairy Cattle - 2.3 mg/lb (5 mg/kg): for the treatment and control of: Lungworms (Adult Dictrocoulus vivingerus: Stomach worms: Adult brown stomach worms (Ostertagia Aduit Derivolations viripatios, stomaderi wortins: Aduit on trom Stomaeri, wortins to User eigita sciertagi). Aduit and fourth stage larvee barberpole worms (Hamonchus contortus & H. placei), and Aduit and fourth stage larvee small stomach worms (Trichostromy)lus avei, Interstitute worms (Gentandiaturi stage) larvee). The howeverse (Burotostomus pheboto-timestitute) worms (Gentandiaturi). The howeverse (Burotostomus pheboto-tication phebotostom) and the stage larvee and the store of the st

o nooular worms (lossopragosionnum radiatum). ef Cattle Only - 4.6 mg/lb (10 mg/kg): for the treatment and control of: Stomach worms h stage inhibited larvae): Ostertagia ostertagi (Type II Ostertagiasis); Tapeworms:

Do not use in dairy cattle at 10 mg/kg.

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

#### DIRECTIONS: Horses and Beef and Dairy Cattle:

Animal \

100

200

300

1000

1500

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.

Veight	Dose (5 mg/kg)	Dose (10 mg/kg)
lb	2.3 mL	4.6 mL
lb	4.6 mL	9.2 mL
lb	6.9 mL	13.8 mL
lb	9.2 mL	18.4 mL
lb	11.5 mL	23.0 mL
lb	23.0 mL	46.0 mL
lb	34.5 mL	69.0 mL

Do not underdose. Ensure each animal receives a complete dose based on a current body weight. Underdosing may result in ineffective treatment, and encourage the development of parasite resistance.

VARNINGS: NOT FOR USE IN HUMANS. KEEP OUT OF REACH OF CHILDREN. The Safety Data Sheet (SDS) contains more detailed occupational safety information. For customer service, adverse effects reporting, and/or a copy of the SDS, call 1-800-211-3573. for additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDAVETS, <u>http://www.fda.gov/reportanimalae</u>.

contact FDA at 1-888-FDAVETS, <u>http://www.tda.gov/report.animalae.</u> **OTHER WARNINGS:** Do not use in horses: intended for human consumption. Parasite resistance may develop to any dewormer, and has been reported for most classes of dewormers. Treatment with a dewormer used in conjunction with parasite management practices appropriate to the geographic area and the animal(s) to be treated may slow the development of parasite resistance. Fecal examinations or other diagnostic tests and parasite management history should be used to determine if the product is appropriate or the herd, prior to the use of any dewormer. Following the use of any dewormer, effectiveness of treatment should be monitored (for example, with the use of a fecal egg count reduction test or another appropriate method). A decrease in a drug's affectiveness over time as calculated by fecal egg count reduction tests may indicate the development of resistance to the dewormer administered. Vour parasite management plan should be adgusted accordingly based on regular monitoring.

endazole (active ingred.) made in China. Formulated in France

Intervet Inc. (d/b/a Merck Animal Health), Madison, NJ 07940

Approved by FDA under NADA # 104-494

Approved by FDA under NADA # 128-620

©2020 Intervet Inc., a subsidiary of Merck & Co. Inc.

1,000 mL (33.8 fl.oz.) 328771 R8 312522 R11

Rev. 11/20

(SELENIUM, VITAMIN E

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. DESCRIFTION: BO-SE seleniom, vitamin JB BO-SE Seleniom, vitamin JE is an emulsion of selenium-tocopherol Deficiency syndrome in calves, lambs, and weeks, and sa an aid in the prevention and treatment of Selenium-Tocopherol Deficiency in sows and veaning pigs. Each **mL contains**: 21 9 mg sodium selenitle (equivalent to 1 mg selenium), 50 mg (Bg USP units) vitamin E (as *d*-alpha tocopheryl acetate), 250 mg polysorbate 80, 2% benzyl acohol (preservative), water for injection q.s. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH.

hydrochlóric acid may be added to adjust pH. PHARMACOLOGY: III has been demostrated that selenium and tocopherol exert physiological effects and that these effects are intertwined with suffur metabolism. Additi onall yoto pher ol appears to have a si gni fi cant r ol ein t heax i dati on por c ess. thus suggesting an intertelationship between selenium and tocopherol in overcoming suffur 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 suffur and, perhaps, other factors interfere during the digestive processwith proper utilization of selenium and tocopherol. When selenium and tocopherol are injected, they typass the digestive process and exert their full metabolic effects promptly on cell metabolism. Anti-inflammany action has been demonstrated by selenium-cochperol in the Selye Pouch Technique and experimentally induced polyarthritis study in rats.

INDICATIONS: BBO-SE (selenium, vitamin E) is recommended for the prevention and INDICATIONS: BBO-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 unthriftness, upmonary distess and/or cardiac arrest. In sows and weaning pigs, as an aid in the prevention and treatment of diseases associated with Selenium-Toco pherol deficiency, such as hepatic necrosis, multiparty 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 pregnance

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. Selenium-Vitamin E preparations can be toxic when improperly administered.



RESIDUE WARNINGS: 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.



PRECAUTIONS: Selenium-Tocopherol Deficiency (STD) syndrome produces a variety and PrecEqUIUMS: Selenum-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 SCOT, and creatine levels may serve as airks in arriving at a diagnosis of STD, when associated with other indices. Selenium is toxic if administred in access. A fixed does schedule is therefore important (read package insert for each selenium-tocopherol modul carefully before using).

product carefully before using). ADVERSE REACTIONS: Reactions, including acute respiratory distress, frothing from the nose and mouth, bloating, severe depression, abortions, and deaths have occurred in pregnant exes. Do not use product with phase separation or turbidity DOSAGE ADD DOMINISTRATION: Inject subuanceously on 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. Tant per 40 pounds of body weight (innimum, Tin). Exes: 2.5 mL per 100 pounds of body weight. Sows: T mL per 40 pounds of body weight. Weanling pigs: T mL per 40 pounds of body weight (minimum, 1 mL). Not for use in newborn pigs. nL). Not for use in n orn pigs

Store at 35°C (77°F) with excursions permitted between 23 - 32°C (74 - 89°F). Use within 90 days of first puncture and puncture a maximum of 12 times. If more than 12 punctures are anticipated, the use of multi-dosing equipment is recommended. When using a draw-off spike or needle with bore diameter larger than 16G, discard any product remaining in the viail immediately after use.

Occasionally, the product may segregate in two phases or may become turbid. Do not use product that has exhibited phase separation or turbidity. HOW SUPPLIED: 100 mL sterile, multiple dose vial, NDC 0061-0807-05.

Approved by FDA under NADA # 012-635

Copyright ©2020 Intervet Inc., A subsidiary of Merck and Co., Inc. Madison, NJ 07940, All rights reserved.

Made in Germany. Rev. 12/20

#### MU-SE°

Intervet /Merck Anim PRODUCT INFORMATION

NADA # 30-314, Approved by FDA (SELENIUM, VITAMIN E)

Injection

For Veterinary Use Only

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

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. DIRECTIONS: MU-SE (selenium, vitamin E) is an emulsion of selenium-tocopherol for the prevent of Selenium-tocopherol Beficiency (STD) syndrome in weaning 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 (sa d-alpha tocopheryl actatel, 250 mg polysorbate 80, 2% benzyl alcohol (preservative), water for injection or a.5 sodium Mydroxide and/or hydroxchoir caid 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 of access that preserve the restoring promain metabolism. Athough 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 in overcoming the digestive process with proper utilization of selenium and tocopherol. When selenium and tocopherol are injected, they bypass the digestive process and exert ther full metabolism. It is apparent that be explaned bechnicus and exerces and exert ther full metabolism to fetces prompty on cell metabolism. Anti-inflammatory action has been demonstrated by selenium tocopherol in the Selve Pouch Technicus and exercementally induced obarthritis tavid vir nats. Selve Pouch Technique and expe mentally induced polyarthritis study in rate

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; unth

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 preg

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 does schedule is therefore important (read package insert for each selenium-locopherol product carefully before usina).

PRECAUTIONS: Selenium-Tocopherol Deficiency (STD) syndrome produces a variety and complexity of symptoms often interfering with a proper diaposits. 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. Server meslenium 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.

Copyright © 1985, 1996, 1998, 2015, Intervet Inc., a subsidiary of Merck & Co., Inc., Madison, NJ 07940. All rights reserved.

Made in Germany. Rev 03/15

138188 R1

CPN: 1047131.3

# Merck Animal Health is invested in your success.

We work hard every day to arm you with the latest science, knowledge, technology and products to support the health of your dairy on multiple levels. Our comprehensive product lines for everyday needs, coupled with robust technical expertise, real-world technology applications and other value-added services allow us to support you in a way no other company can. That's Merck Animal Health.

MAHCattle.com



MAHCattle.com  $\bullet$  800-521-5767 © 2022 Merck & Co., Inc., Rahway, NJ, USA and its affiliates. All rights reserved: 10/22 US All other marks are the property of their respective owners.