MERCK
Animal Health

SWINE
PRODUCT GUIDE

DRIVEN BY PREVENTION®

We're driven by prevention.

They say an ounce of prevention is worth a pound of cure. That's never been more true than now. Here at Merck Animal Health, we have always been and continue to be driven by prevention.

Why? Because it's the right thing to do. Both for animal welfare and for operational efficiency.

That means proactively focusing on solving swine production challenges now and into the future. While it starts with a proven lineup of the disease prevention and reproductive options you need to be successful at every stage, it also means continuing to innovate, supporting our customers and the industry, and bringing new thinking and solutions to an ever-changing market.

Because our goal is to help ensure the healthier pigs you need to propel your business forward.

DrivenByPrevention.com

BIRTH TO FINISH PRODUCTS FOR PIG HEALTH	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5 OR OLDER
 **ARGUS® SC/ST** **Avirulent Live Culture – 500 dose, 10x100 dose** An aid in the prevention of pneumonia, diarrhea, septicemia and mortality caused by *Salmonella* Choleraesuis and as an aid in control of disease and shedding of *Salmonella* Typhimurium. For mass application of pigs 3 weeks of age or older through the drinking water. (See complete label instructions.) Unique dual-strain protection and safety. Freeze-dried avirulent live culture.			OR		
 **CIRCUMVENT® PCV G2** **With MICROSOL DILUVAC FORTE® – 50 dose, 250 dose** An aid in the prevention of viremia, an aid in the reduction of virus shedding and an aid in the reduction of lymphoid infection caused by porcine circovirus Type 2. Convenient dosing options (one x 2 mL or two x 1 mL) for one-dose and two-dose programs. (See complete label instructions.) The only PCV2 vaccine approved for use in pigs as early as 3 days of age (two-dose option). Five-month PCV2 Duration of Immunity (DOI).	IM	**Two-Dose Option:** *1 mL at 3 days of age or older, followed by second 1 mL 3 weeks later.*	IM	**One-Dose Option:** *2 mL once at 3 weeks of age or older.*	
 **CIRCUMVENT® PCV-M G2** **With MICROSOL DILUVAC FORTE® – 50 dose, 250 dose** An aid in the prevention of viremia, an aid in the reduction of virus shedding, an aid in the reduction of lymphoid infection caused by porcine circovirus Type 2 and an aid in the reduction of lung lesions caused by *Mycoplasma hyopneumoniae*. Convenient dosing options (one x 2 mL or two x 1 mL) for one-dose and two-dose programs. (See complete label instructions.) The only PCV2 vaccine approved for use in pigs as early as 3 days of age (two-dose option). Five-month PCV2 DOI.	IM	**Two-Dose Option:** *1 mL at 3 days of age or older, followed by second 1 mL 3 weeks later.*	IM	**One-Dose Option:** *2 mL once at 3 weeks of age or older.*	
 **M+PAC®** **With EMUNADE® – 50 dose, 250 dose** An aid in the prevention of pneumonia caused by *Mycoplasma hyopneumoniae* infection in swine. Convenient one- or two-dose options (one x 2 mL and two x 1 mL) for one-dose and two-dose programs. (See complete label instructions.) Unique patented dual-emulsion adjuvant. Up to four months DOI with a single shot.	IM or SQ	**Two-Dose Option:** *1 mL at 7-10 days of age or older, followed by second 1 mL 2 weeks later.*	IM or SQ		**One-Dose Option:** *2 mL once at 6 weeks of age or older.*
 **MYCO SILENCER® ONCE** **With MICROSOL DILUVAC FORTE® – 250 dose** An aid in the prevention of pneumonia caused by *Mycoplasma hyopneumoniae* infection in swine. Convenient one- or two-dose options (one x 2 mL and two x 1 mL) for one-dose and two-dose programs. (See complete label instructions.) Unique patented dual-emulsion adjuvant. Up to six months DOI with a single shot.			IM	**Two-Dose Option:** *Second 1 mL shot given 2-3 weeks after first 1 mL shot.* *(Second shot not required if 2 mL shot is given at week 3.)*	IM
 **PORCILIS® ILEITIS** **With MICROSOL DILUVAC FORTE® – 50 dose, 250 dose** An aid in the control of ileitis caused by *Lawsonia intracellularis*, an aid in the reduction of colonization by *Lawsonia* and an aid in the reduction of duration of fecal shedding. Convenient dosing options (one x 2 mL or two x 1 mL) for one-dose and two-dose programs as early as 3 days of age (two-dose option). (See complete label instructions.) DOI for at least 20 weeks has been demonstrated.	IM	**Two-Dose Option:** *1 mL at 3 days of age or older, followed by second 1 mL 3 weeks later.*	IM	**One-Dose Option:** *2 mL once at 3 weeks of age or older.*	
 **PRIME PAC® PRRS RR** **Modified Live Virus (MLV) – 20 dose, 100 dose** This product has been shown to be effective for the vaccination of healthy swine 3 weeks of age or older against respiratory disease caused by Porcine Reproductive and Respiratory Syndrome (PRRS) virus and female breeding age swine against reproductive disease caused by PRRS virus. For sows and gilts, inject a single 1 mL dose intramuscularly eight weeks prior to breeding, and for piglets, inject a single 1 mL dose IM at 3 weeks of age or older. (See complete label instructions.) Freeze-dried MLV vaccine with diluent.			IM		
 **PROSYSTEM® ROTA** **Modified Live Virus (MLV) – 50 dose** An aid in the prevention of rotaviral diarrhea in young pigs; a 1-mL oral dose and 1-mL IM dose to pig preweaning. (See complete label instructions.) Unique rotavirus protection includes two major serotypes – G4 and G5 – of serogroup A. Freeze-dried MLV vaccine with diluent.		IM and OR *(7-10 days preweaning)*			

KEY

IM	OR	SQ
INTRAMUSCULAR INJECTION	ORAL ADMINISTRATION	SUBCUTANEOUS INJECTION

PRE-BREEDING
PRODUCTS FOR REPRODUCTION EFFICIENCY AND HEALTH

MATRIX®
(altrenogest) – 2.2 mg/mL

OR

Allows synchronization of estrus (heat), so gilt pool can be brought into heat when it is convenient and efficient. For synchronization of estrus in sexually mature gilts that have had at least one estrous cycle. Treatment with altrenogest solution 0.22% results in estrus (standing heat) four to nine days after completion of the 14-day treatment period. (See complete label instructions.)

IMPORTANT SAFETY INFORMATION: Gilts must not be slaughtered for human consumption for 21 days after the last treatment. Do not use in gilts having a previous or current history of uterine inflammation. Underfeeding of MATRIX® (altrenogest) Solution 0.22% may lead to the occurrence of cystic follicles. Avoid skin contact. Wear vinyl, neoprene, or nitrile protective gloves when handling this product. DO NOT USE LATEX GLOVES. Pregnant women or women who suspect they are pregnant should not handle MATRIX®. Women of childbearing age should exercise extreme caution when handling this product. Accidental absorption could lead to a disruption of the menstrual cycle or prolongation of pregnancy. People who should not handle this product include those with thrombophlebitis, thromboembolic disorders, or with a history of these events, cerebral-vascular or coronary-artery disease, suspected estrogen-dependent neoplasia, benign or malignant tumors which developed during the use of oral contraceptives or other estrogen containing products, liver dysfunction or disease, and women with known or suspected carcinoma of the breast or undiagnosed vaginal bleeding. Wash off accidental spillage on the skin immediately with soap and water. For complete safety information, refer to the product label.

P.G. 600®
[serum gonadotropin (PMSG) and chorionic gonadotropin (HCG)]

IM

Maximizes pig flow by helping more gilts and weaned sows cycle, particularly in summer, producing more pigs when market prices are high.[1,2] For induction of fertile estrus (heat) in healthy prepuberal (non-cycling) gilts over 5½ months of age and weighing at least 187 lbs. For induction of estrus in healthy weaned sows experiencing delayed return to estrus. (See complete label instructions.)

[1]Induction and Synchronization of Estrus in Prepuberal Gilts and Anestrous Sows by a PMSG/HCG-Compound Technical Report No. 9.

[2]The Attainment of Estrus in Sows Administered with 400 I.U. Pregnant Mare Serum Gonadotropin and 200 I.U. Human Chorionic Gonadotropin at Weaning.

IMPORTANT SAFETY INFORMATION: Treatment will not induce estrus in gilts that have already reached puberty (begun to cycle). Gilts that are less than five and one-half months of age or that weigh less than 85 kg (187 lb.) may not be mature enough to continue normal estrus cycles or maintain a normal pregnancy to full term after treatment. Treatment will not induce estrus in sows that are returning to estrus normally three to seven days after weaning. Delayed return to estrus is most prevalent after the first litter; the effectiveness of P.G. 600 has not been established after later litters. Delayed return to estrus often occurs during periods of adverse environmental conditions, and sows mated under such conditions may farrow smaller than normal litters. For complete safety information, refer to the product label.

PRE-FARROW
PRODUCTS FOR REPRODUCTION EFFICIENCY AND HEALTH

PROSYSTEM® RCE
Modified Live Virus (MLV) – 25 dose

IM

An aid in prevention of rotaviral diarrhea and enterotoxemia colibacillosis in nursing pigs of vaccinated sows/gilts. Unique rotavirus and seven-way scours protection. Includes two major rotavirus serotypes – G4 and G5 – of serogroup A. Freeze-dried MLV vaccine with bacterin/toxoid diluent. (See complete label instructions.)

PARASITICIDE
PRODUCTS FOR PIG HEALTH

SAFE-GUARD® DEWORMER
20% Type A Medicated Feed Article

OR

For the treatment and control of: **Lungworms:** Adult *Metastrongylus apri*, adult *Metastrongylus pudendotectus*; **Gastrointestinal worms:** Adult and larvae (L3, L4 stages, liver, lung, intestinal forms) large roundworms (*Ascaris suum*), Adult nodular worms (*Oesophagostomum dentatum*, *O. quadrispinulatum*), Adult small stomach worms (*Hyostrongylus rubidus*), Adult and larvae (L2, L3, L4 stages – intestinal mucosal forms) whipworms (*Trichuris suis*); and **Kidney worms:** Adult and larvae *Stephanurus dentatus*. The Safe-Guard Dewormer 20% Type A Medicated Feed article can only be purchased by an approved medicated feed mill. (See complete label instructions.) Ask your Merck Animal Health representative for the various Safe-Guard presentations available from our distributor partners.

WARNING: KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN. NOT FOR USE IN HUMANS. OTHER WARNINGS: Parasite resistance may develop to any dewormer. The parasite management plan should be adjusted accordingly based on regular monitoring. Withdrawal Periods: Swine must not be slaughtered for human consumption within 4 days following last treatment with this drug product. See product label for more information.

SAFE-GUARD® AQUASOL
(fenbendazole oral suspension) – 200 mg fenbendazole/mL

OR

Indicated for swine, except for nursing piglets, for the treatment and control of: **Lungworms:** Adult *Metastrongylus apri*, Adult *Metastrongylus pudendotectus*; **Gastrointestinal worms:** Adult and larvae (L3, L4 stages, liver, lung, intestinal forms) large roundworms (*Ascaris suum*); Adult nodular worms (*Oesophagostomum dentatum*, *O. quadrispinulatum*); Adult small stomach worms (*Hyostrongylus rubidus*); Adult and larvae (L2, L3, L4 stages – intestinal mucosal forms) whipworms (*Trichuris suis*); and **Kidney worms:** Adult and larvae *Stephanurus dentatus*. See Product Information for complete directions and warnings.

IMPORTANT SAFETY INFORMATION: Swine intended for human consumption must not be slaughtered within 2 days of the last treatment. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

SYMPTOMATIC CARE PRODUCTS FOR PIG HEALTH

BANAMINE®-S
(flunixin meglumine injection) – 50 mg/mL

IM

For control of pyrexia (fever) associated with swine respiratory disease. (See complete label instructions.)

IMPORTANT SAFETY INFORMATION: Swine must not be slaughtered for human consumption within 12 days of last treatment. Do not use in animals showing hypersensitivity to flunixin meglumine. Use judiciously, when renal impairment or gastric ulceration is suspected. Not for use in breeding swine. For complete information on Banamine-S Injectable Solution use, contraindications and warnings, see accompanying product package insert.

BIOSECURITY PRODUCTS FOR PIG HEALTH

ARMATREX® ANTIMICROBIAL
A Silane Quaternary Ammonium Salt

EPA-registered for use in livestock and companion animal facilities as a final bacteriostatic finish to impart fungistatic (mold and mildew) or algistatic activity that provides freshness and reduces surface deterioration or microbiologically induced corrosion.

ANTI-INFECTIVE
PRODUCTS FOR PIG HEALTH

AROVYN™
(tulathromycin injection) – 100 mg/mL

IM

AROVYN Injectable Solution is indicated for the treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Bordetella bronchiseptica*, *Haemophilus parasuis* and *Mycoplasma hyopneumoniae* and for the control of SRD associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Mycoplasma hyopneumoniae* in groups of pigs where SRD has been diagnosed. See Product Information for complete directions and warnings.

IMPORTANT SAFETY INFORMATION: The pre-slaughter withdrawal time for AROVYN in swine is five days. AROVYN should not be used in animals known to be hypersensitive to the product.

NUFLOR®-S
(florfenicol) Injectable Solution – 300 mg/mL

IM

The first and only injectable florfenicol approved for use in U.S. swine. For treatment of swine respiratory disease associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella* Choleraesuis, *Streptococcus suis*, *Bordetella bronchiseptica* and *Glaesserella* (*Haemophilus*) *parasuis* in swine except for nursing piglets and swine of reproductive age intended for breeding. See Product Information for complete directions and warnings.

IMPORTANT SAFETY INFORMATION: Do not use in animals intended for breeding purposes. Perianal inflammation, rectal eversion, rectal prolapse and diarrhea may occur transiently following treatment. Swine intended for human consumption must not be slaughtered within 11 days of the last intramuscular treatment. Intramuscular injection may result in trim loss of edible tissue at slaughter. The effects of florfenicol on porcine reproductive performance, pregnancy and lactation have not been determined. Not for human use and keep away from children. Avoid direct contact with skin, eyes, and clothing. Pregnant women should wear gloves and exercise caution or avoid handling this product. See Product Information for Full Prescribing Information.

RNA PARTICLE TECHNOLOGY PRODUCTS FOR PIG HEALTH

SEQUIVITY®

SEQUIVITY®
RNA particle technology

An innovative and highly advanced RNA particle technology that's used to create flexible, safe and precise solutions to new and evolving disease challenges.

This remarkable technology targets specific pathogens to produce customized prescription vaccines against both viral and bacterial pathogens.

The SEQUIVITY platform allows veterinarians and producers to stay ahead of existing and evolving disease challenges such as PCV2, PCV3, rotavirus, influenza and more with a sophisticated dashboard and unparalleled support.

Contact a Merck Animal Health representative or your veterinarian to find out more.

Conditionally licensed vaccines using the SEQUIVITY platform:

Prescription Product, RNA Particle

For vaccination against the organisms and strains listed. This product is a prescription platform veterinary biologic to be used under the supervision of a licensed veterinarian. Efficacy and potency have not been demonstrated.

Porcine Epidemic Diarrhea (PED) Vaccine, RNA Particle Platform PEDV Sequence Variant 002

For the vaccination of healthy swine as a control against disease caused by Porcine Epidemic Diarrhea Virus.

MERCK Animal Health

VACCINE ANTIGEN CHART

● = Indicated Use
■ = Modified Live

	Protection															
	Sows	Pigs	*Clostridium perfringens* Type C	*Escherichia coli* K88, K99, 987P, F41	Influenza	*Lawsonia intracellularis*	*Mycoplasma hyopneumoniae*	Porcine Circovirus Type 2	Porcine Circovirus Type 3	Porcine Epidemic Diarrhea (PED)	PRRSV	*Rotavirus* A	*Rotavirus* B	*Rotavirus* C	*Salmonella* Choleraesuis	*Salmonella* Typhimurium
Circovirus Vaccines																
CIRCUMVENT® PCV G2		●						●								
CIRCUMVENT® PCV-M G2		●					●	●								
Respiratory Vaccines																
MYCO SILENCER® ONCE		●					●									
M+PAC®		●					●									
PRIME PAC® PRRS RR	●	●									■					
Enteric Vaccines																
PORCILIS® ILEITIS		●				●										
ARGUS® SC/ST		●													■	■
PROSYSTEM® RCE	●		●	●							■					
PROSYSTEM® ROTA		●									■					
RNA Particle Technology Vaccines																
SEQUIVITY®*	●				●			●	●	●		●	●	●		

*Talk to a Merck Animal Health representative to learn more about all SEQUIVITY antigens.

RECOMMENDED NEEDLE SIZES AND LENGTHS:

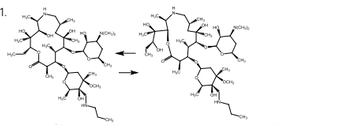
INTRAMUSCULAR INJECTION	GAUGE	LENGTH
Baby Pigs	18 or 20	5/8" or 1/2"
Nursery	16 or 18	3/4" or 5/8"
Finisher	16	1"
Breeding Stock	14 or 16	1" or 1 1/2"
SUBCUTANEOUS INJECTION	**GAUGE**	**LENGTH**
Nursery	16 or 18	1/2"
Finisher	16	3/4"
Breeding Stock	14 or 16	1"

PRODUCT INFORMATION AND LABEL INSTRUCTIONS

AROVYN™
(tulathromycin injection)
Injectable Solution
Antibiotic
100 mg of tulathromycin/mL

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.

DESCRIPTION
AROVYN Injectable Solution is a ready-to-use sterile parenteral preparation containing tulathromycin, a semi-synthetic macrolide antibiotic of the subclass triamilide. Each mL of AROVYN contains 100 mg of tulathromycin, 500 mg propylene glycol, 19.2 mg citric acid and 5 mg monothioglycerol. Sodium hydroxide or hydrochloric acid may be added to adjust pH. AROVYN consists of an equilibrated mixture of two isomeric forms of tulathromycin in a 9:1 ratio. Structures of the isomers are shown below.
Figure 1.



The chemical names of the isomers are [2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino)methyl]-α-L-ribo-hexopyranosyl]oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]-oxy]-1-oxa-6-azacyclopentadecan-15-one and (2R,3R,4R,8R,9R,10S,11S,12R)-11-[[2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino)methyl]-α-L-ribo-hexopyranosyl]oxy]-2-[(1R,2R)-1,2-dihydroxy-1-methylbutyl]-8-hydroxy-3,6,8,10,12-pentamethyl-9-[[3,4,6-trideoxy-3-(dimethylamino)-β-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 disease (BRD) associated with *Mannheimia haemolytica*, *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 haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*.
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 of bovine foot rot (interdigital necrobacillosis) associated with *Fusobacterium necrophorum* and *Porphyromonas levii*.
Suckling Calves, Dairy Calves, and Veal Calves
BRD - AROVYN Injectable Solution is indicated for the treatment of BRD associated with *M. haemolytica*, *P. multocida*, *H. somni*, and *M. bovis*.
Swine
AROVYN Injectable Solution is indicated for the treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Bordetella bronchiseptica*, *Haemophilus parasuis*, and *Mycoplasma hyopneumoniae*; and for the control of SRD associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, and *Mycoplasma hyopneumoniae* in groups of pigs where SRD has been diagnosed.

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

Table 1. AROVYN Cattle Dosing Guide

Animal Weight (Pounds)	Dose Volume (mL)	Animal Weight (Pounds)	Dose Volume (mL)
100	1.1	600	6.8
200	2.3	700	8.0
300	3.4	800	9.1
400	4.5	900	10.2
500	5.7	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	1.7		

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 cows. Use in these cattle may cause drug residues in milk and/or in calves born to these cows.
Swine
Swine intended for human consumption must not be slaughtered within 5 days from the last treatment.

PRECAUTIONS
Cattle
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 reaction that may result in trim loss of edible tissue at slaughter.

ADVERSE 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 EXPERIENCE
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 event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of reporting frequency in cattle: Injection site reactions and anaphylaxis/anaphylactoid reactions. For a complete listing of adverse reactions for tulathromycin injectable solution reported to the CVM see: http://www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY
At physiological pH, tulathromycin (a weak base) is approximately 50 times more soluble in hydrophilic than hydrophobic media. This solubility profile is consistent with the extracellular pathogen activity typically associated with the macrolides.[1] Markedly higher tulathromycin concentrations are observed in the lungs as compared to the plasma. The extent to which lung concentrations represent free (active) drug was not examined. Therefore, the clinical relevance of these elevated lung concentrations is undetermined. Although the relationship between tulathromycin and the characteristics of its antimicrobial effects has not been characterized, as a class, macrolides tend to be primarily bacteriostatic, but may be bactericidal against some pathogens.[2] 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 (MIC) of the targeted pathogen. Under these conditions, the time that serum concentrations remain above the MIC becomes the major determinant of antimicrobial activity. Macrolides also exhibit a post-antibiotic effect (PAE), 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 and exposure time, drug concentration tends to be the most powerful determinant of the duration of PAE. Tulathromycin is eliminated from the body primarily unchanged via biliary excretion.
[1]*Carbon, C. 1998.Pharmacodynamics of Macrolides, Azalides, and Streptogramins: Effect on Extracellular Pathogens. Clin. Infect. Dis., 27:28-32.*
[2]*Nightingale, C.J. 1997. Pharmacokinetics and P harmacodynamics of Newer Macrolides. Pediatr. Infect. Dis. J., 16:438-443.*
Cattle
Following subcutaneous administration into the neck of feeder calves at a dosage of 2.5 mg/kg BW, 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 11 L/kg in healthy ruminating calves.[1] This extensive volume of distribution is largely responsible for the long elimination half-life of this compound [approximately 2.75 days in the plasma (based on quantifiable terminal plasma drug concentrations) versus 8.75 days for total lung concentrations (based on data from healthy animals)]. Linear pharmacokinetics are observed with subcutaneous doses ranging from 1.27 mg/kg BW to 5.0 mg/kg BW. No pharmacokinetic differences are observed in castrated male versus female calves.
[1]*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, tulathromycin is completely and rapidly absorbed (T_{max} ~0.25 hour). Subsequently, the drug rapidly distributes into body tissues, achieving a volume of distribution exceeding 1 L/kg. The free drug is rapidly cleared from the systemic circulation ($Cl_{systemic}$ = 187 mL/hr/kg). However, it has a long terminal elimination half-life (60 to 90 hours) owing to its extensive volume of distribution. Although pulmonary tulathromycin concentrations are substantially higher than concentrations observed in the plasma, the clinical significance of these findings is undetermined. There are no gender differences in swine tulathromycin pharmacokinetics.

MICROBIOLOGY
Cattle
Tulathromycin has demonstrated *in vitro* activity against *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*, four pathogens associated with BRD; against *Moraxella bovis* associated with IBK; and against *Fusobacterium necrophorum* and *Porphyromonas levii* associated with bovine 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 by the CLSI (M11-A6). All MIC values were determined using the 9:1 isomer ratio of this compound.
BRD – The MICs of tulathromycin were determined for BRD isolates obtained from calves enrolled in therapeutic and at-risk field studies in the U.S. in 1999. In the therapeutic studies, isolates were obtained from pretreatment nasopharyngeal swabs from all study calves, and from lung swabs or lung tissue of saline-treated calves that died. In the at-risk studies, isolates were obtained from nasopharyngeal swabs of saline-treated non-responders, and from lung swabs or lung tissue of saline-treated calves that died. The results are shown in Table 3.
IBK – 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 pre-treatment conjunctival swabs of calves with clinical signs of IBK enrolled in the tulathromycin 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 *Porphyromonas levii* obtained from cattle enrolled in foot rot field studies in the U.S. and Canada in 2007. Isolates were obtained from pretreatment 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.

Table 3. Tulathromycin minimum inhibitory concentration (MIC) values* for indicated pathogens isolated from field studies evaluating BRD and IBK in the U.S. and from foot rot field studies in the U.S. and Canada.

Indicated pathogen	Date isolated	No. of isolates	MIC_{50}** (ug/mL)	MIC_{90}** (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	≤ 0.063 to > 64
Moraxella bovis	2004	55	0.5	0.5	0.25 to 1
Fusobacterium necrophorum	2007	116	2	64	≤ 0.25 to > 128
Porphyromonas levii	2007	103	8	128	≤ 0.25 to > 128

* 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.

Swine
In vitro activity of tulathromycin has been demonstrated against *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Bordetella bronchiseptica*, *Haemophilus parasuis*, and *Mycoplasma hyopneumoniae*. The MICs of tulathromycin against indicated SRD pathogens were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLSI, M31-A and M31-A3). MICs for *Haemophilus parasuis* were determined using Veterinary Fastidious Medium and were incubated 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 tulathromycin 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 BRD and IBK in the U.S. and from foot rot field studies in the U.S. and Canada.

Indicated pathogen	Date isolated	No. of isolates	MIC_{50}** (ug/mL)	MIC_{90}** (ug/mL)	MIC range (ug/mL)
Actinobacillus pleuropneumonia	2002-2002 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	2002-2002 2007-2008	55 40	1 1	2 2	0.5 to > 64 ≤ 0.03 to > 2
Bordetella bronchiseptica	2002-2002	42	4	8	2 to 8

* 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
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°F on 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 saline-treated calves.
Fifty-two tulathromycin injection-treated calves and 27 saline-treated calves from the multi-location field BRD treatment study had *Mycoplasma bovis* identified in cultures from pre-treatment nasopharyngeal swabs. Of the 52 tulathromycin injection-treated calves, 37 (71.2%) calves were categorized as cures and 15 (28.8%) calves were categorized as treatment failures. Of the 27 saline-treated calves, 4 (14.8%) calves were categorized as 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 older 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 young calves was at least as good as the BRD treatment success rate in older calves. As a result, tulathromycin injection is considered effective 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, administration of tulathromycin 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 attitude/activity, normal respiration, and a rectal temperature of ≤ 104°F on Day 14. There were no BRD-related deaths in the tulathromycin injection-treated calves compared to two BRD-related deaths in the saline-treated calves. Fifty saline-treated calves classified as non-responders in this study had *Mycoplasma bovis* identified in cultures of post-treatment nasopharyngeal swabs or lung tissue.
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 had 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 BRD 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-treated calves compared with saline-treated calves (11.3% vs. 28.9%, P = 0.0001 and 15.0% vs. 30.7%, P < 0.0001).
IBK – Two field studies were conducted evaluating tulathromycin injection for the treatment of IBK associated with *Moraxella bovis* in 200 naturally-infected calves. 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 eyes, 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 cure rate was significantly higher (P < 0.05) for tulathromycin injection-treated calves compared to saline-treated calves. Additionally, time to improvement was significantly less (P < 0.0001) in both studies for tulathromycin injection-treated calves compared to saline-treated calves.
Foot Rot – 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 subcutaneous dose of tulathromycin 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 tulathromycin injection-treated calves compared with saline-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 < 104°F on Day 7. The treatment success rate was significantly greater (P ≤ 0.05) in tulathromycin injection-treated pigs (70.5%) compared to saline-treated pigs (46.1%). *M. hyopneumoniae* was isolated from 106 saline-treated and non-treated sentinel pigs in this study.
Two induced infection model studies were conducted to confirm the effectiveness of tulathromycin injection against *M. hyopneumoniae*. Ten days after inoculation intranasally and intratracheally with a field strain of *M. hyopneumoniae*, 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 effectiveness of tulathromycin injection for the control of SRD was evaluated in a multi-location natural infection field study. When at least 15% of the study candidates showed clinical signs of SRD, all pigs were enrolled and treated with tulathromycin injection (226 pigs) or saline (227 pigs). Responses to treatment were evaluated on Day 7. Success was defined as a pig with normal attitude, normal respiration, and rectal temperature of < 104°F. The treatment success rate was significantly greater (P < 0.05) in tulathromycin injection-treated pigs compared to saline-treated pigs (59.2% vs. 41.2%).

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 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 showed signs of resolving over time. No other drug-related lesions were observed macroscopically or microscopically. An exploratory study was conducted in feeder calves receiving a single subcutaneous dose of 10, 12.5, or 15 mg/kg BW. Macroscopically, no lesions were observed. Microscopically, minimal to mild myocardial degeneration was seen in one of six calves administered 12.5 mg/kg BW and two of six calves administered 15 mg/kg BW.
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 or microscopically.
Swine
Safety studies were conducted in pigs receiving a single intramuscular dose of 25 mg/kg BW, or 3 weekly intramuscular doses of 2.5, 7.5, or 12.5 mg/kg BW. In all groups, transient indications of pain after injection were seen, including restlessness 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 changes were seen in animals at all dosages and resolved over time. No other drug-related lesions were observed 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 syringe is recommended. When using a draw-off spike 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
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 http://www.fda.gov/reportanimalae.

TAKE TIME OBSERVE LABEL DIRECTIONS

MERCK Animal Health

Rev: 12/21

BANAMINE®-S
(FLUNIXIN MEGLUMINE INJECTION (50 MG/ML))

For intramuscular use in swine.

Veterinary Not for use in breeding swine.

NADA #101-479, Approved by FDA.

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

DESCRIPTION: Each milliliter of BANAMINE-S (flunixin meglumine injection) contains 50 mg flunixin (equivalent to 83 mg flunixin 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 preservative, hydrochloric acid, water for injection q.s.

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

Flunixin is known to persist in inflammatory tissues[1] and is associated with anti-inflammatory properties which extend well beyond the period associated with detectable plasma drug concentrations[2]. Therefore, prediction of drug concentrations based upon 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.

The pharmacokinetic profiles were found to follow a 2-compartmental model, although a deep (third) compartment was observed in some animals. The mean terminal elimination half-life (ß half-life) of flunixin after a single intramuscular injection of Banamine (2.2 mg/kg) to pigs was between 3 and 4 hours. The mean observed maximum plasma concentration was 2944 ng/mL, achieved at a mean time of approximately 0.4 hours. The mean $AUC_{(0-LOQ)}$ was 6431 ng*hr/mL. Following IM administration of flunixin, quantifiable drug concentration could be measured up to 18 hours post dose. The mean volume of distribution was 2003 mL/kg and the mean total clearance was 390 mL/hr/kg. The mean absolute bioavailability of flunixin following an intramuscular injection in the neck was 87%.

INDICATION: BANAMINE-S (flunixin meglumine injection) is indicated for the control of pyrexia associated with swine respiratory disease.

DOSE AND ADMINISTRATION: The recommended dose for swine is 2.2 mg/kg (1 mg/lb; 2 mL per 100 lbs) body weight given by a single intramuscular administration. The injection should be given only in the neck musculature with a maximum of 10 mL per site.

USE WITHIN 28 DAYS OF FIRST PUNCTURE AND PUNCTURE A MAXIMUM OF 10 TIMES. WHEN USING A DRAW-OFF SPIKE OR NEEDLE WITH BORE DIAMETER LARGER THAN 18 GAUGE, DISCARD ANY PRODUCT REMAINING IN THE VIAL IMMEDIATELY AFTER USE.

Note: Intramuscular injection may cause local tissue irritation and damage. In an injection-site irritation study, the tissue damage did not resolve in all animals by Day 28 post-injection. This may result in trim loss of edible tissue at slaughter.

CONTRAINDICATIONS: There are no known contraindications to this drug in swine when used as directed. Do not use in animals showing hypersensitivity to flunixin meglumine. Use judiciously when renal impairment or gastric ulceration is suspected.

RESIDUE WARNINGS: SWINE MUST NOT BE SLAUGHTERED FOR HUMAN CONSUMPTION WITHIN 12 DAYS OF THE LAST TREATMENT.

PRECAUTIONS: As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Patients at greatest risk for adverse events are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed.

Since many NSAIDs possess the potential to produce gastrointestinal ulceration, concomitant use of flunixin meglumine with other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided.

Not for use in breeding swine. The reproductive effects of BANAMINE-S (flunixin meglumine injection) have not been investigated in this class of swine.

Intramuscular injection may cause local tissue irritation and damage. In an injection site irritation study, the tissue damage did not resolve in all animals by Day 28 post-injection. This may result in trim loss of edible tissue at slaughter.

ADVERSE REACTIONS: Flunixin was mildly irritating at the injection sites. No other flunixin-related changes (adverse reactions) were noted in swine administered a 1X (2.2 mg/kg; 1.0 mg/lb) dose for 9 days.

ANIMAL SAFETY: Minimal toxicity manifested itself as statistically significant increased spleen weight at elevated doses (5X or higher daily for 9 days) with no change in normal microscopic architecture.

HOW SUPPLIED: BANAMINE-S (flunixin meglumine injection), 50 mg/mL is available in 100-mL (NDC # 0061-1838-30) multi-dose vials.

Store at or below 25°C (77°F). Do not freeze.

See the In-Use statement as provided in the Dose and Administration section.

REFERENCES:

1. Lees P, Higgins AJ. Flunixin inhibits prostaglandin E_2 production in equine inflammation. *Res Vet Sci.* 1984; 37:347-349.
2. Oldensvik K. Pharmacokinetics of flunixin and its effect on prostaglandin $F_{2\alpha}$ alpha metabolite concentrations after oral and intravenous administration in heifers. *J Vet Pharmacol Ther.* 1995; 18:254-259.

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

Made in Germany.
Rev. 01/17

MATRIX®
(ALTRENOGEST SOLUTION 0.22% (2.2 MG/ML))

FOR USE IN ANIMALS ONLY
Net Contents: 1000 mL

DRUG FACTS:

Active ingredients: Altrenogest solution 0.22% (2.2 mg/mL)

Use: For synchronization of estrus in sexually mature gilts that have had at least one estrous cycle. Treatment with altrenogest solution 0.22% results in estrus (standing heat) 4 to 9 days after completion of the 14-day treatment period.

Caution: Federal law prohibits extra-label use of this drug to enhance food and/or fiber production in animals.

Do Not Use: In gilts having a previous or current history of uterine inflammation (i.e., acute, subacute or chronic endometritis).

Restricted Drug (California) - use only as directed. Not for Human Use

Manufactured for: Intervet Inc (d/b/a Merck Animal Health), Madison, NJ 07940 a subsidiary of Merck & Co.

WARNINGS:

User/Handler Safety:

Keep this and all medication out of the reach of children. Avoid skin contact. Wear vinyl, neoprene or nitrile protective gloves when handling this product. DO NOT USE LATEX GLOVES. Pregnant women or women who suspect they are pregnant should not handle MATRIX® (altrenogest) Solution 0.22%. Women of childbearing age should exercise extreme caution when handling this product. Accidental absorption could lead to a disruption of the menstrual cycle or prolongation of pregnancy. Wash off accidental spillage on the skin immediately with soap and water.

People who should not handle this product:
1. Women who are or suspect they are pregnant.
2. Anyone with thrombophlebitis or thromboembolic disorders or with a history of these events.
3. Anyone with cerebral-vascular or coronary-artery disease.
4. Women with known or suspected carcinoma of the breast.
5. People with known or suspected estrogen-dependent neoplasia.
6. Women with undiagnosed vaginal bleeding.
7. People with benign or malignant tumors which developed during the use of oral contraceptives or other estrogen containing products.
8. Anyone with liver dysfunction or disease.

Accidental exposure: Altrenogest is readily absorbed from contact with the skin. In addition, this oil based product can penetrate porous gloves. Altrenogest should not penetrate intact vinyl, neoprene or nitrile protective gloves; however, if there is leakage (i.e., pinhole, spillage, etc.) the contaminated area covered by such occlusive materials may have increased absorption. DO NOT USE LATEX GLOVES

The following measures are recommended in case of accidental exposure.

Skin Exposure: Wash immediately with soap and water.

Eye Exposure: Immediately flush with plenty of water for 15 minutes. Get medical attention.

If Swallowed: Do not induce vomiting. MATRIX® (altrenogest) Solution 0.22% contains an oil. Call a physician. Vomiting should be supervised by a physician because of possible pulmonary damage via aspiration of the oil base. If possible, bring the container and labeling to the physician.

Effects of Overexposure: There has been no human use of this specific product. The information contained in this section is extrapolated from data available on other products of the same pharmacological class that have been used in humans. Effects anticipated are due to the progestational activity of altrenogest. Acute effects after a single exposure are possible; however, continued daily exposure has the potential for more untoward effects such as disruption of the menstrual cycle, uterine or abdominal cramping, increased or decreased uterine bleeding, prolongation of pregnancy and headaches. The oil base may also cause complications if swallowed. In addition, the list of people who should not handle this product is based upon the known effects of progestins used in humans on a chronic basis.

HUMAN FOOD SAFETY: GILTS MUST NOT BE SLAUGHTERED FOR HUMAN CONSUMPTION FOR 21 DAYS AFTER THE LAST TREATMENT.

Environmental Safety: Place empty drug containers, waste from rinsing the dosing gun, protective gloves or other articles that come in contact with this product in a leak-resistant container for disposal in accordance with applicable Federal, state and local regulations.

Adverse Reactions and Potential Safety Hazards: Underfeeding of MATRIX® may lead to the occurrence of cystic follicles.

When Using This Product: A small percentage (less than 5%) of treated gilts may exhibit estrus (standing heat) during the 14-day treatment period. Gilts nearing estrus at the start of the 14-day treatment period may express estrus early in that period.

Dosage and Directions: While wearing protective gloves, remove shipping cap and seal; replace with enclosed plastic dispensing cap. Connect the Matrix® Dosing Device to the solution bottle according to the dosing device instructions provided as an attachment to the Matrix® Dosing Device package. Administer 6.8 mL (15 mg altrenogest) per gilt once daily for 14 consecutive days. Treat gilts on an individual animal basis by top-dressing MATRIX® on a portion of each gilt's daily feed allowance. To produce the desired synchronization of estrus in a group of gilts, treat all of the gilts daily for the same 14-day period.

Other Information:

Storage: Store Matrix® solution bottle and dosing device when loaded with solution for continued use at or below room temperature, 77°F (25°C). Close tightly.

Questions? Comments?
- To report adverse reaction call Merck at 1-800-211-3573.
- To obtain product information, including material safety data sheet (MSDS), call 1-800-441-8272.
- For additional information about adverse drug experience for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/Animal/Veterinary/SafetyHealth

www.merck-animal-health-usa.com

NADA #141-222, Approved by FDA

PRODUCT INFORMATION

361060 R1

Approved by FDA under NADA # 141-063

Nuflor®-S (FLORFENICOL)

Injectable Solution 300 mg/mL

For intramuscular use in swine except for nursing piglets and swine of reproductive age intended for breeding.

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

DESCRIPTION: Nuflor®-S Injectable Solution is a sterile solution of the synthetic, broad-spectrum antibiotic florfenicol. Each milliliter of sterile Nuflor®-S Injectable Solution contains 300 mg of florfenicol, 250 mg *N*-methyl-2-pyrrolidone (NMP), 150 mg propylene glycol and polyethylene glycol q.s.

INDICATIONS: Nuflor®-S Injectable Solution is indicated for treatment of swine respiratory disease associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella* Choleraesuis, *Streptococcus suis*, *Bordetella bronchiseptica*, and *Glaesserella (Haemophilus) parasuis* in swine except for nursing piglets and swine of reproductive age intended for breeding.

DOSAGE AND ADMINISTRATION: Nuflor®-S Injectable Solution should be administered by intramuscular injection to swine at a dose rate of 15 mg/kg (1 mL/45 lb) body weight. A second dose should be administered 48 hours later. The injection should be given only in the neck musculature. If a positive response is not noted within 24 hours after the second injection, the diagnosis should be re-evaluated, and/or an alternative treatment may be considered. Administered dose volume should not exceed 10 mL per injection site.

Nuflor®-S DOSAGE GUIDE FOR SWINE	
ANIMAL WEIGHT (lbs)	IM Nuflor®-S DOSAGE (1 mL/ 45 lb Body Weight) (mL)
22	0.5
45	1
90	2
135	3
180	4
225	5
270	6

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains materials that can be irritating to skin and eyes. Avoid direct contact with skin, eyes and clothing. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. Reproductive and developmental toxicities have been reported in laboratory animals following high, repeated exposures to 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.

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 online at www.fda.gov/reportanimalae.

PRECAUTIONS: Not for use in animals intended for breeding purposes. The effects of florfenicol on porcine reproductive performance, pregnancy and lactation have not been determined.

Intramuscular injection in swine may result in local tissue reaction which could persist up to 21 days post-dosing. This may result in trim loss of edible tissue at slaughter.

RESIDUE WARNINGS: Swine intended for human consumption must not be slaughtered within 11 days of the last intramuscular treatment.

ADVERSE REACTIONS: Perianal inflammation, rectal eversion, rectal prolapse and diarrhea may occur transiently following treatment. Decreased feed and water consumption may occur if the labeled dosage regimen is exceeded.

CLINICAL PHARMACOLOGY: The pharmacokinetic disposition of florfenicol was evaluated in 20 pigs following a single IM injection of Nuflor®-S at the labeled dose of 15 mg/kg BW. The mean ± standard deviation maximum plasma concentration (C_{max}) and the time to reach C_{max} (T_{max}) of florfenicol were 3.42 ± 0.82 µg/mL and 4.70 ± 2.15 hours, respectively. The mean ± standard deviation area under the drug concentration-time curve between times 0 and the last quantifiable concentration ($AUC_{0\text{-}LOQ}$) and the terminal half-life ($T_{1/2}$) of florfenicol were 70.34 ± 23.78 µg*hours/mL and 11.21 ± 3.73 hours, respectively.

MICROBIOLOGY: Florfenicol is a synthetic, broad-spectrum antibiotic active against many Gram-negative and Gram-positive bacteria isolated from domestic animals. It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis. Florfenicol is generally considered a bacteriostatic drug, but exhibits bactericidal activity against certain bacterial species.

In vitro activity of florfenicol has been demonstrated against commonly isolated pathogens associated with swine respiratory disease. Isolates tested were obtained from pre-treatment lung samples from representative non-enrolled pigs at each study site and post-treatment lung samples from pigs in the florfenicol-treated and saline-treated groups that died or were euthanized during the study, or were classified as treatment failures at the end of the study. The minimum inhibitory concentrations (MICs) of florfenicol for swine respiratory pathogens from clinical studies were determined using dilution methods. These susceptibility test methods were adequately controlled with the inclusion and acceptable performance of appropriate reference strains. The results are presented in Table 1.

Table 1. Florfenicol minimum inhibitory concentration (MIC) values* for indicated target pathogens isolated from a multi-site field study evaluating swine respiratory disease in the U.S. in 2001.

Indicated pathogens	Number of Isolates	MIC_{50} ** (µg/mL)	MIC_{90} ** (µg/mL)	MIC Range (µg/mL)
Actinobacillus pleuropneumoniae	100	0.25	0.5	0.25-1
Pasteurella multocida	107	0.5	0.5	0.25-0.5
Bordetella bronchiseptica	49	2	2	0.5-4
Glaesserella parasuis	36	0.5	0.5	≤0.12-1.0
Streptococcus suis	62	2	2	1-2
Salmonella Choleraesuis	36	4	4	2-4

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

EFFECTIVENESS: In a multi-site natural infection field study, a total of 620 growing pigs with clinical signs of SRD (rectal temperature of ≥ 104.5°F, and a depression score (on a scale of 0 [absent] to 3 [severe]) of ≥ 2, and a dyspnea score (on a scale of 0 [absent] to 3 [severe]) of ≥ 2) were treated with either florfenicol (15 mg/kg BW IM given on Days 0 and 2) or an equivalent volume of saline. Treatment success (rectal temperature of < 104°F, and a depression score of 0 or 1, and a dyspnea score of 0 or 1) was evaluated on Day 6. The treatment success rate was statistically significantly different ($p < 0.0001$) and higher in the florfenicol-treated group (72%) than in the saline-treated control group (33.1%).

ANIMAL SAFETY: A safety study was conducted in 40 healthy crossbred growing pigs. Pigs were administered florfenicol by IM injection in the neck at 1X, 3X, or 5X the labeled dose (15, 45, or 75 mg/kg BW, respectively) for 3X the labeled duration of treatment (6 injections at 48-hour intervals), or 10X the labeled dose (150 mg/kg BW) administered as two injections 48 hours apart. Test article-related diarrhea (moderate), anal swelling/erythema (mild to moderate), and injection site swelling (mild to moderate) were seen in all florfenicol-treated groups after dosing, most frequently in the 3X and 5X groups. Although these findings were considered clinically relevant, the incidence and severity in the 1X group was considered within acceptable limits. Test article-related decreases in feed and water consumption and an associated decrease in body weight were seen in the 3X and 5X groups. Test article-related changes in some serum chemistry parameters and decreased numbers of white blood cells were seen in the 3X, 5X, and/or 10X groups; the changes were generally minimal and not considered clinically significant. Most changes in drug-related, in-life parameters did not become apparent until after dosing was extended beyond the labeled duration of two injections, 48 hours apart.

Injection site irritation was evaluated in a safety study using 20 healthy crossbred growing pigs administered florfenicol at 15 mg/kg BW IM in the neck as two injections 48 hours apart. Mild injection site swelling was seen in up to approximately 32% of the pigs by 4 days post-injection and was resolved by 16 days post-injection. Gross and histopathologic evaluation showed that injection site discoloration and inflammation was present at 7 and 14 days post-injection, and absent at 21, 28, and 42 days post-injection.

STORAGE CONDITIONS: Store between 2-30°C (36-86°F). Do not store above 30°C (86°F). Protect from light when not in use. Use within 30 days of first puncture and puncture a maximum of 30 times. If more than 30 punctures are anticipated, the use of multi-dosing equipment is recommended. When using a draw-off spike or needle with bore diameter larger than 18 gauge, discard any product remaining in the vial immediately after use.

HOW SUPPLIED: Nuflor®-S (florfenicol) Injectable Solution is packaged in 100 mL glass sterile multiple dose vials.

Approved by FDA under NADA # 141-063
Florfenicol (active ingred.) made in China.
Formulated in Germany.

Rev. 09/2021

MERCK Animal Health

P.G. 600®

NADA NO. 140-856; APPROVED BY FDA

FOR ANIMAL USE ONLY

DESCRIPTION

Gilts normally reach puberty (begin experiencing normal estrous cycles and exhibiting regular estrus or heat) at any time between six and eight months of age, although some gilts will not have exhibited their first estrus at ten months of age. Age at first estrus is influenced by several factors including breed type, season of the year, environmental conditions, and management practice (Hurtgen, 1986).

Sows normally exhibit estrus three to seven days after weaning their litters; however, some otherwise healthy sows may not exhibit estrus for 30 days or more after weaning (Dial and Britt, 1986). The causes of delayed return to estrus in healthy sows are poorly understood, but probably include season of the year (so-called seasonal anestrus; Hurtgen, 1979), adverse environmental conditions, such as high ambient temperatures (Love, 1978), and the number of previous litters, because the condition is more prevalent after the first litter than after later litters (Hurtgen, 1986).

P.G. 600 is a combination of serum gonadotropin (Pregnant Mare Serum Gonadotropin or PMSG) and chorionic gonadotropin (Human Chorionic Gonadotropin or HCG) for use in prepuberal gilts (gilts that have not yet exhibited their first estrus) and in sows at weaning. It is supplied in freeze-dried form with sterile diluent for reconstitution.

In gilts and sows, the action of serum gonadotropin is similar to the action of Follicle-Stimulating Hormone (FSH), which is produced by the animals' anterior pituitary gland. It stimulates the follicles of the ovaries to produce mature ova (eggs), and it promotes the outward signs of estrus (heat).

The action of chorionic gonadotropin in gilts and sows is similar to the action of Luteinizing Hormone (LH), which is also produced by the animals' anterior pituitary gland. It causes the release of mature ova from the follicles of the ovaries (ovulation), and it promotes the formation of corpora lutea, which are necessary for the maintenance of pregnancy once the animals have become pregnant.

The combination of serum gonadotropin and chorionic gonadotropin in P.G. 600 induces fertile estrus in most prepuberal gilts and weaned sows three to seven days after administration (Schilling and Cerne, 1972; Britt et al., 1986; Bates et al., 1991). The animals may then be mated or, in the case of gilts, mating may be delayed until the second estrus after treatment.

NOTE: P.G. 600 IS INTENDED AS A MANAGEMENT TOOL TO IMPROVE REPRODUCTIVE EFFICIENCY IN SWINE PRODUCTION OPERATIONS. TO OBTAIN MAXIMUM BENEFIT FROM THIS PRODUCT, ESTRUS DETECTION AND OTHER ASPECTS OF REPRODUCTIVE MANAGEMENT MUST BE ADEQUATE. IF YOU ARE IN DOUBT ABOUT THE ADEQUACY OF YOUR BREEDING PROGRAM, CONSULT YOUR VETERINARIAN.

PG. 600 is available in two package sizes:

SINGLE DOSE VIALS (order Code No. PG-720-1) - Five vials containing white freeze-dried powder, plus five vials containing sterile diluent. When reconstituted, each single dose vial (5 mL) of P.G. 600 contains:

SERUM GONADOTROPIN (PMSG)	400 IU
CHORIONIC GONADOTROPIN (HCG)	200 IU
(equivalent to 200 USP Units chorionic gonadotropin)	

FIVE DOSE VIALS (order Code No. PG-720-5) - One vial containing white freeze dried powder, and one vial containing sterile diluent. When reconstituted, the five dose vial (25 mL) of P.G. 600 contains:

SERUM GONADOTROPIN (PMSG)	2000 IU
CHORIONIC GONADOTROPIN (HCG)	1000 IU
equivalent to 1000 USP Units chorionic gonadotropin	

INDICATIONS FOR USE

PREPUBERAL GILTS: P.G. 600 is indicated for induction of fertile estrus (heat) in healthy prepuberal (non-cycling) gilts over five and one-half months of age and weighing at least 85 kg (187 lb.).

SOWS AT WEANING: P.G. 600 is indicated for induction of estrus in healthy weaned sows experiencing delayed return to estrus.

CAUTIONS

Treatment will not induce estrus in gilts that have already reached puberty (begun to cycle). Gilts that are less than five and one-half months of age or that weigh less than 85 kg (187 lb.) may not be mature enough to continue normal estrus cycles or maintain a normal pregnancy to full term after treatment.

Treatment will not induce estrus in sows that are returning to estrus normally three to seven days after weaning. Delayed return to estrus is most prevalent after the first litter; the effectiveness of P.G. 600 has not been established after later litters. Delayed return to estrus often occurs during periods of adverse environmental conditions, and sows mated under such conditions may farrow smaller than normal litters.

DOSAGE AND ADMINISTRATION

One dose (5 mL) of reconstituted P.G. 600, containing 400 IU serum gonadotropin (PMSG) and 200 IU chorionic gonadotropin (HCG), should be injected into the gilt or sow's neck behind the ear.

Prepuberal gilts should be injected when they are selected for addition to the breeding herd. Sows should be injected at weaning during periods of delayed return to estrus.

DIRECTIONS FOR USE

SINGLE DOSE VIALS: Using a sterile syringe and a sterile 0.90 x 38 mm (20 G x 1½") hypodermic needle, transfer the contents of one vial of sterile diluent (5 mL) into one vial of freeze-dried powder. Shake gently to dissolve the powder. Inject the contents of the vial into the gilt or sow's neck behind the ear.

FIVE DOSE VIAL: Using a sterile syringe and a sterile 0.90 x 38 mm (20 G x 1½") hypodermic needle, transfer approximately 5 mL of the sterile diluent into the vial of freeze-dried powder. Shake gently to dissolve the powder. Transfer the dissolved product back into the vial of diluent and shake gently to mix. Inject one dose (5 mL) of the reconstituted solution into the gilt or sow's neck behind the ear.

STORAGE PRECAUTIONS

Store at 36-46°F (2-8°C).

Once reconstituted, P.G. 600 should be used immediately. Unused solution should be disposed of properly and not stored for future use. Spent hypodermic needles and syringes generated as a result of the use of this product must be disposed of properly in accordance with all applicable Federal, State and local regulations.

REFERENCES

Bates, R.O., B.N. Day, J.H. Britt, L.K. Clark and M.A. Brauer (1991). Reproductive performance of sows treated with a combination of Pregnant Mare's Serum Gonadotropin and Human Chorionic Gonadotropin at weaning in the summer. Journal of Animal Science 69:894.

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Madison, NJ, 07940 USA

by:
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UNTERSCHLEISSHEIM, GERMANY

Rev. 9/16

MERCK Animal Health

SAFE-GUARD® DEWORMER

(20% TYPE A MEDICATED ARTICLE)

MUST BE MIXED BEFORE FEEDING ACCORDING TO DIRECTIONS AND PERMITTED CLAIMS.
FOR USE IN MANUFACTURED FEEDS ONLY.
ACTIVE DRUG INGREDIENT: Fenbendazole 200 grams per kilogram (90.7 grams per pound).
INERT INGREDIENTS: Roughage Products or Roughage Products and Calcium Carbonate; and Mineral Oil.

FOR THE TREATMENT AND CONTROL OF:
Lungworms: Adult *Metastrongylus apri*, adult *Metastrongylus pudendotectus*; **Gastrointestinal worms:** Adult and larvae (L3, L4 stages, liver, lung, intestinal forms) large roundworms (*Ascaris suum*), Adult nodular worms (*Oesophagostomum dentatum, O. quadrispinulatum*), Adult small stomach worms (*Hyostrongylus rubidus*), Adult and larvae (L2, L3, L4 stages - intestinal mucosal forms) whipworms (*Trichuris suis*); and **Kidney worms:** Adult and larvae *Stephanurus dentatus*.

DRUG FEEDING RATE:
9 mg fenbendazole per kg body weight (4.08 mg fenbendazole per pound) to be fed as the sole ration over a period of 3 to 12 days.

MIXING DIRECTIONS:
Thoroughly mix SAFE-GUARD® 20% Type A medicated article with non-medicated swine feed according to the table below to obtain the proper concentration in the Type B medicated feed. The following table gives examples of how some Type B medicated feed concentrations can be prepared:

Swine Type B Medicated Feed Instructions	
Pounds of Type A Medicated Article to Add per Ton of Feed to Make a Type B Medicated Feed	Resulting Fenbendazole Concentration in Type B Medicated Feed [grams/ton (grams/pound)]
11.03	1,000 (0.5)
195.59	17,740 (8.9)

Thoroughly mix SAFE-GUARD® 20% Type A medicated article with non-medicated swine feed according to the table below to obtain the proper concentration in the complete Type C medicated feed. Prepare an intermediate pre-blend of the Type A medicated article prior to mixing in a complete feed. Thoroughly mix the required amount of Type A medicated article in a convenient quantity of feed ingredients (a dilution of one part Type A medicated article and nine parts grain carrier is suggested), then thoroughly mix this pre-blend with the rest of the feed ingredients to ensure complete and uniform distribution of the Type A medicated article.

The following table gives examples of how some complete Type C medicated feeds can be prepared:

Swine Type C Medicated Feed Instructions	
Pounds of Type A Medicated Article to Add per Ton to Make a Type C Medicated Feed	Resulting Fenbendazole Concentration in Type C Medicated Feed [grams/ton (grams/pound)]
0.11	10 (0.005)
3.31	300 (0.15)

FEEDING DIRECTIONS:
Feed as the sole ration for three (3) to twelve (12) consecutive days. No prior withdrawal of feed or water necessary.
Type C medicated swine feeds containing SAFE-GUARD® 20% can be fed pelleted or as a meal.

WARNING: KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN. NOT FOR USE IN HUMANS. 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, or http://www.fda.gov/reportanimalae.

OTHER WARNINGS: Parasite resistance may develop to any dewormer. All dewormers require accurate dosing for best results. Following the use of any dewormer, effectiveness of treatment should be monitored. A decrease of effectiveness over time may indicate the development of resistance to the dewormer administered. The parasite management plan should be adjusted accordingly based on regular monitoring.

***Withdrawal Periods*:** Swine must not be slaughtered for human consumption within 4 days following last treatment with this drug product.

CONSULT YOUR VETERINARIAN FOR ASSISTANCE IN THE DIAGNOSIS, TREATMENT, AND CONTROL OF PARASITISM.
STORE AT OR BELOW 25°C (77°F). EXCURSIONS UP TO 40°C (104°F) ARE PERMITTED.

SAFE-GUARD® AQUASOL

(FENBENDAZOLE ORAL SUSPENSION)
SUSPENSION CONCENTRATE, ANTIPARASITIC

APPROVED BY FDA UNDER NADA # 141-449

200 MG FENBENDAZOLE/ML

For oral administration via drinking water

DESCRIPTION: Safe-Guard® AquaSol is a suspension concentrate containing fenbendazole, an antiparasitic. Each mL of Safe-Guard® AquaSol contains 200 mg of fenbendazole.

INDICATIONS:
Chickens: Safe-Guard® AquaSol is indicated for the treatment and control of adult *Ascaridia galli* in broiler chickens and replacement chickens and for the treatment and control of adult *A. galli* and *Heterakis gallinarum* in breeding chickens and laying hens.

Swine: Safe-Guard® AquaSol is indicated for swine, except for nursing piglets, for the treatment and control of: **Lungworms:** Adult *Metastrongylus apri*, Adult *Metastrongylus pudendotectus*; **Gastrointestinal worms:** Adult and larvae (L3, L4 stages, liver, lung, intestinal forms) large roundworms (*Ascaris suum*); Adult nodular worms (*Oesophagostomum dentatum, O. quadrispinulatum*); Adult small stomach worms (*Hyostrongylus rubidus*); Adult and larvae (L2, L3, L4 stages - intestinal mucosal forms) whipworms (*Trichuris suis*), and Kidney worms: Adult and larvae *Stephanurus dentatus*.

DOSAGE AND ADMINISTRATION:
Chickens: Safe-Guard® AquaSol must be administered orally to chickens via the drinking water at a daily dose of 1 mg/kg BW (0.454 mg/lb) for 5 consecutive days.

Swine: Safe-Guard® AquaSol must be administered orally to swine via the drinking water at a daily dose of 2.2 mg/kg BW (1 mg/lb) for 3 consecutive days.

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

GENERAL MIXING DIRECTIONS:
Chickens:
Dose calculation:
The daily dose of 1 mg fenbendazole per kg BW (0.454 mg/lb) is equivalent to 0.005 mL Safe-Guard® AquaSol per kg BW (0.00227 mL/lb). The required daily volume of product is calculated from the total estimated body weight [kg] of the entire group of chickens to be treated. Please use the following formula:

Total estimated body weight [kg] of the chickens to be treated x 0.005 mL = mL Safe-Guard® AquaSol/day

Examples:

Total body weight of birds to be treated	Volume of Safe-Guard® AquaSol per day.	Volume of Safe-Guard® AquaSol (for 5 days)
5,000 kg (11,000 lb)	25 mL	5 x 25 mL = 125 mL
10,000 kg (22,000 lb)	50 mL	5 x 50 mL = 250 mL
80,000 kg (176,000 lb)	400 mL	5 x 400 mL = 2,000 mL
320,000 kg (704,000 lb)	1,600 mL	5 x 1,600 mL = 8,000 mL

Follow the instructions in the order described below to prepare the medicated water. The medicated water must be prepared daily prior to each administration.

Swine:
Dose calculation:
The daily dose is 2.2mg fenbendazole per kg BW (1 mg/lb) which is equivalent to 0.011mL Safe-Guard® AquaSol per kg BW (0.0045 mL/lb).The required daily volume of product is calculated from the total estimated body weight [kg] of the entire group of pigs to be treated. Please use the following formula:

Total estimated body weight [kg] of the pigs to be treated x 0.011mL = mL Safe-Guard® AquaSol/day

Examples:

Total body weight of pigs to be treated	Volume of Safe-Guard® AquaSol per day.	Volume of Safe-Guard® AquaSol (for 3 days)
10,000kg (22,000 lb)	110 mL	3 x 110mL = 330 mL
80,000kg (176,000 lb)	880 mL	3 x 880mL = 2640 mL
320,000 kg (704,000 lb)	3520 mL	3 x 3520mL = 10,560 mL

Follow the instructions in the order described below to prepare the medicated water. The medicated water must be prepared daily prior to each administration.

Prepare a 1 to 1 dilution (pre-dilution) of Safe-Guard AquaSol in water:
1) Calculate the volume of Safe-Guard® AquaSol to be administered daily.
2) Select a measuring device capable of accurately measuring a volume of at least twice the calculated Safe-Guard® AquaSol daily volume.
[Note: If the total volume of the 1 to 1 dilution needed exceeds the volume of the largest available measuring device, divide the total volume into two or more smaller batches of 1 to 1 dilution, prepared following the steps below. Safe-Guard® AquaSol should always be measured by adding it to a measuring device that already contains an equivalent volume of water.]
3) Pour a volume of water equal to the calculated volume of product needed into the measuring device.
4) Shake the product well before mixing.
5) Fill up the measuring device containing the water with the calculated volume of the product to obtain the 1 to 1 dilution.
[Note: If more than the required amount of the product is accidently poured into the measuring device, discard the entire contents and repeat the process from Step 3 above.]
6) Add the 1 to 1 dilution of Safe-Guard® AquaSol in water to the water supply system as described below. Be careful to avoid any accidental spill or loss of 1 to 1 dilution which may inadvertently result in less than the required dose of fenbendazole.
7) Rinse the container used to prepare the 1 to 1 dilution of Safe-Guard® AquaSol with additional water, and add the rinse water to the medicated water tank or the stock suspension tank of the dosing pump.

For use with a medication tank:
Add the entire 1 to 1 dilution of Safe-Guard® AquaSol in water to the medication tank containing the volume of drinking water usually consumed by the animals in 3 to 24 hours. Stir the medicated water in the medication tank until the medicated water is visibly homogeneous. The medicated water should appear hazy. No further stirring during administration is necessary.

For use with a dosing pump:
Add the entire 1 to 1 dilution of Safe-Guard® AquaSol in water to the water in the stock suspension tank of the dosing pump. The volume of water in the stock suspension container has to be calculated taking as a basis the present injection rate of the dosing pump and the volume of drinking water usually consumed by the animals over a period of 3 to 24 hours. Stir until the content in the stock suspension tank is visibly homogeneous. The medicated water should appear hazy.

At concentrations of up to 5 mL/L stock suspension (1 g fenbendazole/L) no stirring is required. At concentrations from 5 mL up to 75 mL of product /L stock suspension (1,000 mg to 15,000 mg fenbendazole/L) and within up to 8 hours during the treatment administration period no stirring of the stock suspension is required. If the administration period exceeds 8 hours, but being no longer than 24 hours, the stock suspension container needs to be equipped with a stirring device.

During treatment, all animals must have sole and unrestricted access to the medicated water. After complete consumption of the medicated water, the animals should have access to non-medicated drinking water *ad libitum*. Ensure that the total amount of medicated water offered is consumed.

USER SAFETY WARNINGS: Not for use in humans. Keep out of reach of children. Protective gloves should be used and care should be taken when handling the product to avoid skin and eye exposure and accidental ingestion. Accidental exposure may result in skin and eye irritation. Accidental ingestion may cause gastrointestinal disturbances and hypersensitivity reactions in humans. 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 http://www.fda.gov/AnimalVeterinary/SafetyHealth.

RESIDUE WARNING: ***Chickens:*** No withdrawal period is required when used according to labeling.
Swine: Swine intended for human consumption must not be slaughtered within 2 days from the last treatment.

OTHER WARNINGS: Parasite resistance may develop to any dewormer. All dewormers require accurate dosing for best results. Following the use of any dewormer, effectiveness of treatment should be monitored. A decrease of effectiveness over time may indicate the development of resistance to the dewormer administered. The parasite management plan should be adjusted accordingly based on regular monitoring.

EFFECTIVENESS:
Chickens: Six pivotal dose confirmation studies and five field effectiveness studies were conducted to evaluate the effectiveness of Safe-Guard® AquaSol oral suspension against adult *A. galli* in broiler chickens and replacement chickens and against *A. galli* and *H. gallinarum* in breeding chickens and laying hens. Safe-Guard® AquaSol was administered orally in drinking water at 1 mg fenbendazole/kg body weight/day for 5 consecutive days. The chickens were necropsied 7 to 8 days after the last treatment, and adult worms in the intestines and ceca of the chickens in the control and treated groups were counted to determine percent efficacy.

Three dose confirmation studies were conducted in European Union (EU), using 105 Rhode Island Red breed hens (2 years old) for each study. In all three studies, the efficacy against *A. galli* (97.9%, 97.3%, and 93.9%) and *H. gallinarum* (99.8%, 96.9%, and 97.3%) was greater than 90%. A fourth dose confirmation study was conducted in the United States (US) using 264 Rhode Island Red breed hens (12 months old). In the study, the efficacy against adult *A. galli* and *H. gallinarum* was 98.7% and 99.2%, respectively. A fifth dose confirmation study was conducted in the US using 176 Cobb breed broiler chickens (4 to 5 weeks old). In the study, the efficacy against adult *A. galli* was 99.4%. A sixth dose confirmation study was conducted in the US using 176 Ross breed broiler chickens (4 to 5 weeks old). In the study, the efficacy against adult *A. galli* was 100%.

A field effectiveness study was conducted in the EU in a flock of 13,244 Hy-Line layer breed replacement chickens (13 weeks old). Fifteen chickens were necropsied before treatment initiation, and 15 chickens were necropsied seven days after treatment for worm counts. The efficacy against adult *A. galli* was 90.2%. A second field effectiveness study was conducted in the US using 550 Ross breed broiler chickens (4 to 5 weeks old). The efficacy against adult *A. galli* was 100%. A third field effectiveness study was conducted in the US using 550 White Leghorn breed replacement chickens (14 weeks old). The efficacy against adult *A. galli* and *H. gallinarum* was 100% and 88.9%, respectively. A fourth field effectiveness study was conducted in the US using 550 Cobb breed breeder hens (63 weeks old). The efficacy against adult *A. galli* and *H. gallinarum* was 97.6% and 95.3%, respectively. A fifth effectiveness study was conducted in the US using 550 Cobb breed broiler chickens (4 to 5 weeks old). The efficacy against adult *A. galli* was 100%.

The pivotal dose confirmation studies and field effectiveness studies demonstrated substantial evidence of effectiveness of Safe-Guard® AquaSol at the dose of 1 mg fenbendazole/kg body weight/day for 5 consecutive days against adult A. galli in broiler chickens and replacement chickens and against adult *A. galli* and *H. gallinarum* in breeding chickens and laying hens.

Swine: A multi-site, masked, negative-controlled dose confirmation field study was conducted to provide substantial evidence of the effectiveness of Fenbendazole (FBZ) Suspension (20% w/v) administered orally in drinking water to pigs for three consecutive days to provide a dose of 2.2 mg FBZ/kg body weight daily against the dose-limiting worm *Trichuris suis* (*T. suis*). A common protocol was implemented in two different geographical locations and with two different investigators.

Weaned, growing-finishing pigs of approximately 6 weeks of age were used in the study. Each study site selected pigs from one source herd verified to be free of *T. suis* infection. Barrow and gilt breeds representative of U.S. commercial production were used. Housing, management, and husbandry procedures were typical of commercial production practice. A complete feed, adequate to meet the nutritional needs of the study animals, was offered to the animals in self-feeders throughout the study. The feed did not contain antibiotics, anthelmintics, or any other medication.

Fifty-six days prior to treatment administration, all suitable study candidates were orally dosed with approximately 4000 embryonated *T. suis* eggs. A natural field isolate of *T. suis* collected in April 2010 from a sow located on a commercial farrow to wean operation located in the U.S. was used. Individual fecal samples were obtained from each candidate animal 46, 47, and 48 days after *T. suis* inoculation and analyzed for the presence of *T. suis* eggs. Animals with at least two fecal examinations positive for *T. suis* eggs were eligible for inclusion in the study.

In each study, 24 healthy pigs were randomized to two treatment groups (FBZ treated and non-medicated) by first blocking by weight in blocks of 4 pigs each and within each weight block, fecal egg count (FEC) in blocks of 2 pigs. The two pigs with the two lowest FEC counts within a weight block were randomized one per treatment group and the two pigs with the highest FEC counts within a weight block were randomized one per treatment group. The two animals assigned to the same treatment group within the same weight block were then assigned to the same pen. Six pens of 2 pigs each were used per treatment group.

Non-medicated water consumption of the pigs in each treatment pen was measured prior to treatment administration to estimate the amount of water required for dosing on each day of the treatment period. The amount of FBZ Suspension administered in drinking water to the study pigs was calculated from pre-treatment body weights. Medicated water was prepared on each treatment day by diluting FBZ Suspension in drinking water to provide a daily dose of 2.2 mg FBZ/kg body weight to the FBZ treated group. The control group received non-medicated drinking water.

Only two pigs at the Minnesota (MN) site that were treated with FBZ had abnormal post-treatment observations ("loose stools"). These two pigs had exhibited abnormal fecal consistency prior to treatment with FBZ. There were no abnormal observations made at the California (CA) site on pigs after FBZ administration. There were no abnormal post-treatment observations attributed to administration of FBZ at either study site. The study animals were euthanized after either 8 or 9 days following the last FBZ administration for retrieval of the large intestinal tract. Adult *T.suis* worms attached to the tract and in the contents of the tract were counted.

Adequacy of infection was demonstrated at both study sites by having more than 6 non-medicated pigs (11 of the 12 non-medicated animals in MN and 9 of the 12 non-medicated animals in CA) with adult *T. suis* worm counts of 100 or more per animal.

There was a significant treatment effect in *T. suis* worm counts between medicated and non-medicated treatment groups at each study site (p=0.0006 in MN and p=0.0003 in CA). The percent reduction in *T. suis* worm counts in the FBZ medicated animals was greater than 90% (98.5% in MN and 98.6% in CA) compared to the non-medicated animals using transformed data (geometric means).

Palatability: A pivotal palatability study was conducted to evaluate the palatability of 20% Fenbendazole Suspension in pigs through voluntary consumption of medicated water when offered for approximately 5 hours a day over 3 consecutive days at a dose of 2.2 mg fenbendazole/kg body weight (BW) per day (label dose). The average percent of medicated water consumed was 98.18%, thus the study demonstrated that 20% Fenbendazole Suspension has acceptable palatability.

ANIMAL SAFETY:
Chickens: Two margin of safety studies (growing broiler chickens and laying hens at peak egg production) and one reproductive safety study (broiler breeder chickens) were conducted. These studies supported the safety of Safe-Guard® AquaSol in broiler chickens, replacement chickens, laying hens and breeding chickens when administered in drinking water at 1 mg fenbendazole/kg body weight/day for 5 consecutive days.

The margin of safety in broiler chickens was conducted in 480 broiler chickens. Safe-Guard® AquaSol was administered orally as medicated drinking water to three groups of 120 chickens (60 male and 60 female in each group) at 1, 3, and 5 mg fenbendazole/kg body weight/day (1, 3, and 5 times the recommended label dose) for 15 consecutive days (3 times the recommended duration). Another group of 120 chickens (60 male and 60 female) was provided non-medicated drinking water and used as a control group. In all chickens, feed and water intake, body weights, clinical health, and mortality were recorded. Hematology and clinical chemistry parameters were evaluated in 24 chickens from each group. At the end of the treatment phase, gross necropsies were performed on 48 chickens from each group, and organs weights were evaluated. Histopathologic examinations were performed on 48 chickens each from the control and 5 mg fenbendazole/kg body weight groups. No clinically significant effects related to the administration of Safe Guard® AquaSol were observed for any of the parameters evaluated.

The margin of safety in laying hens was conducted in 144 laying hens. Safe-Guard® AquaSol was administered orally as medicated drinking water to three groups of 36 hens at 1, 3, and 5 times the recommended label dose (1, 3, and 5 mg fenbendazole/kg body weight/day) for 15 consecutive days (3 times the recommended duration). Another group of 36 hens was provided non-medicated drinking water and used as a control group. In all hens, feed and water intake, body weights, clinical health, mortality, egg production, and egg quality parameters (including egg shell thickness and strength, egg weight, and Haugh unit) were evaluated. Hematology and clinical chemistry parameters were evaluated in 12 hens from each group. At the end of the treatment phase, gross necropsies were performed on 12 hens from each group, and organs weights were evaluated. Histopathologic examinations were performed on 12 hens each from the control and 5 mg fenbendazole/kg body weight groups. No clinically significant effects related to the administration of Safe-Guard® AquaSol were observed for any of the parameters evaluated.

The reproductive safety in broiler breeding chickens was conducted in 220 broiler breeder chickens. Safe-Guard® AquaSol was administered orally as medicated drinking water to a group of 110 breeding chickens (10 male and 100 female) at 3 mg fenbendazole/kg body weight/day (3 times the recommended label dose) for 21 consecutive days (4 times the recommended duration). Another group of 110 breeding chickens (10 male and 100 female) were provided non-medicated drinking water and used as a control group. The parameters evaluated in the study included feed and water intake, body weights, clinical health, egg production and weight, fertility, hatchability, and 14-day old chick viability. Necropsy of unhatched eggs was performed to record the percentage of dead embryos and dead and culled hatchlings. At the end of the treatment phase, 30 breeding chickens (10 male and 20 female) from each group were necropsied; and gross pathology and weights of testes and female reproductive tracts were evaluated. Histopathologic evaluations were performed on the gross lesions collected during the necropsy. No clinically significant effects related to the administration of Safe-Guard® AquaSol were observed for any of the parameters evaluated.

Swine: Animal safety was established using a combination of swine pharmacokinetic, physiologic, and pharmacologic data that provided a basis for bridging the safety data of Safe-Guard® Type A medicated article (NADA 131-675) to Safe-Guard® AquaSol oral suspension in swine.

STORAGE INFORMATION: Store at room temperature 30°C (86°F). Once opened, do not store the container above 25°C (77°F). Do not freeze. Use within 6 months after opening. Use the medicated water within 24 hours.

HOW SUPPLIED: 1 Liter and 1 Gallon (3,785 mL) HDPE plastic containers

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

Use Only as Directed

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

	Distributed by: Intervet Inc. 2 Giralda Farms Madison, NJ 07940

Approved by FDA under NADA # 141-449

Revision Date: 02/21

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