# UNIPRIM- trimethoprim and sulfadiazine powder Neogen Corporation

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#### UNIPRIM POWDER FOR HORSES

#### **DESCRIPTION**

UNIPRIM POWDER FOR HORSES contains 67 mg trimethoprim and 333 mg sulfadiazine per gram.

UNIPRIM POWDER FOR HORSES is a combination of trimethoprim and sulfadiazine in the ratio of 1 part to 5 parts by weight, which provides effective antibacterial activity against a wide range of bacterial infections in animals.

Trimethoprim is 2, 4 diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine.

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#### **ACTIONS**

*Microbiology:* Trimethoprim blocks bacterial production of tetrahydrofolic acid from dihydrofolic acid by binding to and reversibly inhibiting the enzyme dihydrofolate reductase.

Sulfadiazine, in common with other sulfonamides, inhibits bacterial synthesis of dihydrofolic acid by competing with *para*-aminobenzoic acid.

Trimethoprim and sulfadiazine thus imposes a sequential double blockade on bacterial metabolism. This deprives bacteria of nucleic acids and proteins essential for survival and multiplication, and produces a high level of antibacterial activity which is usually bactericidal.

Although both sulfadiazine and trimethoprim are antifolate, neither affects the folate metabolism of animals. The reasons are: animals do not synthesize folic acid and cannot, therefore, be directly affected by sulfadiazine; and although animals must reduce their dietary folic acid to tetrahydrofolic acid, trimethoprim does not affect this reduction because its affinity for dihydrofolate reductase of mammals is significantly less than for the corresponding bacterial enzyme.

Trimethoprim and sulfadiazine is active against a wide spectrum of bacterial pathogens, both gramnegative and gram-positive. The following *in vitro* data are available, but their clinical significance is unknown. In general, species of the following genera are sensitive to trimethoprim and sulfadiazine:

Very Sensitive	<u>Sensitive</u>	<b>Moderately Sensitive</b>	Not Sensitive
Escherichia	Staphylococcus	Moraxella	Mycobacterium
Streptococcus	Neisseria	Nocardia	Leptospira
Proteus	Klebsiella	Brucella	Pseudomonas
Salmonella	Fusiformis		Erysipelothrix
Pasteurella	Corynebacterium		
Shigella	Clostridium		

As a result of the sequential double blockade of the metabolism of susceptible organisms by trimethoprim and sulfadiazine, the minimum inhibitory concentration (MIC) of trimethoprim and sulfadiazine is markedly less than that of either of the components used separately. Many strains of bacteria that are not susceptible to one of the components are susceptible to trimethoprim and sulfadiazine. A synergistic effect between trimethoprim and sulfadiazine in combination has been shown experimentally both *in vitro* and *in vivo* (in dogs).

Trimethoprim and sulfadiazine is bactericidal against susceptible strains and is often effective against sulfonamide-resistant organisms. *In vitro* sulfadiazine is usually only bacteriostatic.

The precise *in vitro* MIC of the combination varies with the ratio of the drugs present, but action of trimethoprim and sulfadiazine occurs over a wide range of ratios with an increase in the concentration of one of its components compensating for a decrease in the other. It is usual, however, to determine MICs using a constant ratio of 1 part trimethoprim in 20 parts of the combination.

The following table shows MICs, using the above ratio, of bacteria which were susceptible to both trimethoprim (TMP) and sulfadiazine (SDZ). The organisms are those most commonly involved in conditions for which trimethoprim/sulfadiazine is indicated:

#### AVERAGE MINIMUM INHIBITORY CONCENTRATION (MIC-mcg/mL)

Dagtorio	TMP	SDZ	TMP/SDZ	
Bacteria	Alone	Alone	TMP	SDZ
Escherichia coli	0.31	26.5	0.07	1.31
Proteus species	1.30	24.5	0.15	2.85
Staphylococcus aureus	0.60	17.6	0.13	2.47
Pateurella species	0.06	20.1	0.03	0.56
Salmonella species	0.15	61.0	0.05	0.95
Streptococcus	0.5	24.5	0.15	2.85

The following table demonstrates the marked effect of the trimethoprim and sulfadiazine combination against sulfadiazine-resistant strains of normally susceptible organisms:

# AVERAGE MINIMUM INHIBITORY CONCENTRATION OF SULFADIAZINE-RESISTANT STRAINS (MIC-mcg/mL)

Bacteria	TMP	SDZ	TMP/S	SDZ
Dacterra	Alone	Alone	TMP	SDZ
Escherichia coli	0.32	>245	0.27	5.0
Proteus species	0.66	>245	0.32	6.2

*Susceptibility Testing:* In testing susceptibility to trimethoprim and sulfadiazine, it is essential that the medium used does not contain significant amounts of interfering substances which can bypass the metabolic blocking action, e.g., thymidine or thymine.

The standard SxT disc is appropriate for testing by the disc diffusion method.

*Pharmacology:* Following oral administration, trimethoprim and sulfadiazine is rapidly absorbed and widely distributed throughout body tissues. Concentrations of trimethoprim are usually higher in tissues than in blood. The levels of trimethoprim are high in lungs, kidney, and liver, as would be expected from its physical properties.

Serum trimethoprim concentrations in horses following oral administration indicate rapid absorption of

the drug; peak concentrations occur in 1.5 hours. The mean serum elimination half-life is 2 to 2.5 hours. Sulfadiazine absorption is slower, requiring 2.5 to 6 hours to reach peak concentrations. The mean serum elimination half-life for sulfadiazine is about 4 to 5.5 hours.

Usually, the concentration of an antibacterial in the blood and the *in vitro* MIC of the infecting organism indicate an appropriate period between doses of a drug. This does not hold entirely for trimethoprim and sulfadiazine because trimethoprim, in contrast to sulfadiazine, localizes in tissues and therefore its concentration and ratio to sulfadiazine are higher there than in blood.

The following table shows the average concentration of trimethoprim and sulfadiazine, as measured in either serum or plasma, in twenty-four adult horses observed after a single dose of UNIPRIM POWDER FOR HORSES:

#### AVERAGE SERUM/PLASMA CONCENTRATION (mcg/mL)

Trimethoprim (5 mg/kg)				Sulfa	diazine (2	5 mg/kg)			
1 hr	3 hr	6 hr	10 hr	24 hr	1 hr	3 hr	6 hr	10 hr	24 hr
0.82	0.69	0.36	0.12	< 0.025	9.9	18.8	17.3	9.0	1.6

Excretion of trimethoprim and sulfadiazine is chiefly by the kidneys, by both glomerular filtration and tubular secretion. Urine concentrations of both trimethoprim and sulfadiazine are several fold higher than blood concentrations. Neither trimethoprim nor sulfadiazine interferes with the excretion pattern of the other.

#### INDICATIONS AND USAGE

UNIPRIM POWDER FOR HORSES is indicated in horses where potent systemic antibacterial action against sensitive organisms is required. UNIPRIM POWDER FOR HORSES is indicated where control of bacterial infections is required during treatment of:

A cuto Strangles	Acute Urogenital
Acute Strangles	Infections
Respiratory Tract	Wound Infections and
Infections	Abscesses

UNIPRIM POWDER FOR HORSES is well tolerated by foals.

#### CONTRAINDICATIONS

Trimethoprim and sulfadiazine should not be used in horses showing marked liver parenchymal damage, blood dyscrasias, or in those with history of sulfonamide sensitivity.

#### **WARNING**

Do not use in horses intended for human consumption.

#### ADVERSE REACTIONS

During clinical trials, one case of anorexia and one case of loose feces following treatment with the drug were reported.

Individual animal hypersensitivity may result in local or generalized reactions, sometimes fatal. Anaphylactoid reactions, although rare, may also occur.

Antidote: Epinephrine.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Neogen Corporation at 859-254-1221 or animalsafety.neogen.com.

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.

**Post Approval Experience:** Horses have developed diarrhea during trimethoprim and sulfadiazine treatment, which could be fatal. If fecal consistency changes during trimethoprim and sulfadiazine therapy, discontinue treatment immediately and contact your veterinarian.

#### **PRECAUTION**

Water should be readily available to horses receiving sulfonamide therapy.

#### **ANIMAL SAFETY**

Toxicity is low. The acute toxicity ( $LD_{50}$ ) of trimethoprim and sulfadiazine is more than 5 g/kg orally in rats and mice. No significant changes were recorded in rats given doses of 600 mg/kg per day for 90 days.

Horses treated intravenously with trimethoprim and sulfadiazine 48% injection have tolerated up to five times the recommended daily dose for 7 days or on the recommended daily dose for 21 consecutive days without clinical effects or histopathological changes.

Lengthening of clotting time was seen in some of the horses on high or prolonged dosing in one of two trials. The effect, which may have been related to a resolving infection, was not seen in a second similar trial.

Slight to moderate reductions in hematopoietic activity following high, prolonged dosage in several species have been recorded. This is usually reversible by folinic acid (leucovorin) administration or by stopping the drug. During long-term treatment of horses, periodic platelet counts and white and red blood cell counts are advisable.

#### **TERATOLOGY**

The effect of trimethoprim and sulfadiazine on pregnancy has not been determined. Studies to date show there is no detrimental effect on stallion spermatogenesis with or following the recommended dose of trimethoprim and sulfadiazine.

#### DOSAGE AND ADMINISTRATION

The recommended dosage is 3.75 g UNIPRIM POWDER FOR HORSES per 110 lbs (50 kg) body weight per day. Administer UNIPRIM POWDER FOR HORSES orally once a day in a small amount of palatable feed.

**Dose Instructions:** One **37.5 g** packet is sufficient to treat 1100 lbs (500 kg) of body weight. For the **1125 g** packets and **12** kg boxes, a level, loose-filled 67 cc scoop contains 37.5 g, sufficient to treat 1100 lbs (500 kg) of body weight. For the **200** g, **400** g, and **1200** g jars, and **2000** g pail, two level, loose-filled, 32 cc scoops contain 37.5 g, sufficient to treat 1100 lbs (500 kg) of body weight. Since product contents may settle, gentle agitation during scooping is recommended.

The usual course of treatment is a single, daily dose for 5 to 7 days.

Continue acute infection therapy for 2 or 3 days after clinical signs have subsided.

If no improvement of acute infections is seen in 3 to 5 days, reevaluate the diagnosis.

UNIPRIM POWDER FOR HORSES may be used alone or in conjunction with intravenous dosing. Following treatment with trimethoprim and sulfadiazine 48% injection, therapy can be maintained using oral Powder.

A complete blood count should be done periodically in patients receiving UNIPRIM POWDER FOR HORSES for prolonged periods. If significant reduction in the count of any formed blood element is noted, treatment with UNIPRIM POWDER FOR HORSES should be discontinued.

#### **STORAGE**

Store at or below 25°C (77°F)

#### **HOW SUPPLIED**

UNIPRIM POWDER FOR HORSES is available in 37.5 g packets, 1125 g packets, 200 g jars, 400 g jars, 1200 g jars, 2000 g pails, and 12 kg boxes. Apple Flavored UNIPRIM POWDER FOR HORSES is available in 37.5 g packets, 1125 g packets, 200 g jars, 400 g jars, 1200 g jars, and 2000 g pails.

#### **CAUTION**

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

#### Approved by FDA under ANADA # 200-033

Manufactured by: Neogen Corporation Lexington, KY 40511 USA • 859-254-1221

animalsafety.neogen.com

#### PRINCIPAL DISPLAY PANEL - 400 g jar (Apple Flavored)

NDC: 59051-3011-3 APPLE FLAVORED

#### (trimethoprim and sulfadiazine)

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

#### Approved by FDA under ANADA # 200-033

**Net Contents:** 400 grams

FOR ANIMAL USE ONLY

**Each gram contains:** 67 mg Trimethoprim, 333 mg Sulfadiazine

**Indications:** For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections and abscesses.

**Recommended Dose:** 3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32cc scoops contain 37.5g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.

#### KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

**Warning:** Do not use in horses intended for human consumption.

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animalsafety.neogen.com L3442-0420

Rev. 04/20

Made in the USA

Item No. AUP400

#### FOR ANIMAL USE ONLY

#### Each gram contains:

Trimethoprim 67 mg Sulfadiazine 333 mg

#### Indications:

For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections, and abscesses.

#### Recommended Dose:

3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32 cc scoops contain 37.5 g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.



#### KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

#### Warning:

Do not use in horses intended for human consumption.



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Rev. 04/20 Made in the USA



#### PRINCIPAL DISPLAY PANEL - 200 g jar (Apple Flavored)

NDC: 59051-3011-4 APPLE FLAVORED

**UNIPRIM®** 

**POWDER FOR HORSES** 

(trimethoprim and sulfadiazine)

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

Approved by FDA under ANADA # 200-033

Net Contents: 200 grams
FOR ANIMAL USE ONLY

**Each gram contains:** 67 mg Trimethoprim, 333 mg Sulfadiazine

**Indications:** For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections and abscesses.

**Recommended Dose:** 3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32cc scoops contain 37.5g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.

KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

**Warning:** Do not use in horses intended for human consumption.

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animalsafety.neogen.com L3440-0420

Rev. 04/20

Made in the USA

Item No. AUP200

#### FOR ANIMAL USE ONLY

#### Each gram contains:

Trimethoprim 67 mg Sulfadiazine 333 mg

#### Indications:

For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections, and abscesses.

#### Recommended Dose:

3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32 cc scoops contain 37.5 g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.



#### KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

#### Warning:

Do not use in horses intended for human consumption.



**Manufactured by:** Neogen Corporation Lexington, KY 40511 USA • 859-254-1221 animalsafety.neogen.com L3440-0420

Rev. 04/20 Made in the USA



#### PRINCIPAL DISPLAY PANEL - 1200 g jar (Apple Flavored)

NDC: 59051-3011-5 APPLE FLAVORED

**UNIPRIM®** 

#### POWDER FOR HORSES

(trimethoprim and sulfadiazine)

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

Approved by FDA under ANADA # 200-033

Net Contents: 1200 grams
FOR ANIMAL USE ONLY

Each gram contains: 67 mg Trimethoprim, 333 mg Sulfadiazine

**Indications:** For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections and abscesses.

**Recommended Dose:** 3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32cc scoops contain 37.5g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.

#### KEEP OUT OF REACH OF CHILDREN

#### Store at or below 25°C (77°F)

**Warning:** Do not use in horses intended for human consumption.

Manufactured by: Neogen Corporation

Lexington, KY 40511 USA • 859-254-1221

animalsafety.neogen.com L3405-0420

Rev. 04/20

Made in the USA

Item No. AUP1200

#### FOR ANIMAL USE ONLY

#### Each gram contains:

Trimethoprim 67 mg Sulfadiazine 333 mg

#### Indications:

For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections, and abscesses.

#### Recommended Dose:

3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32 cc scoops contain 37.5 g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.



#### KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

#### Warning:

Do not use in horses intended for human consumption.



Manufactured by: Neogen Corporation Lexington, KY 40511 USA • 859-254-1221 animalsafety.neogen.com L3405-0420

Rev. 04/20 Made in the USA



#### PRINCIPAL DISPLAY PANEL - 2000 g pail (Apple Flavored)

NDC: 59051-3011-6 APPLE FLAVORED

**UNIPRIM®** 

#### **POWDER FOR HORSES**

#### (trimethoprim and sulfadiazine)

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

#### Approved by FDA under ANADA # 200-033

Net Contents: 2000 grams

#### FOR ANIMAL USE ONLY

**Each gram contains:** 67 mg Trimethoprim, 333 mg Sulfadiazine

**Indications:** For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections and abscesses.

**Recommended Dose:** 3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32cc scoops contain 37.5g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.

#### KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

**Warning:** Do not use in horses intended for human consumption.

**Manufactured by:** Neogen Corporation Lexington, KY 40511 USA • 859-254-1221

animalsafety.neogen.com L3441-0420

Rev. 04/20

Made in the USA

Item No. AUP2000

#### FOR ANIMAL USE ONLY

#### Each gram contains:

Trimethoprim 67 mg Sulfadiazine 333 mg

#### Indications:

For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections, and abscesses.

#### Recommended Dose:

3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32 cc scoops contain 37.5 g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package onsert for additional information.



#### KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

#### Warning

Do not use in horses intended for human consumption.

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Rev. 04/20 Made in the USA



#### PRINCIPAL DISPLAY PANEL - 37.5 g pouch (Apple Flavored)

NDC: 59051-3011-1 APPLE FLAVORED

**UNIPRIM®** 

#### POWDER FOR HORSES

#### (trimethoprim and sulfadiazine)

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

Approved by FDA under ANADA # 200-033

Net Contents: 37.5 grams
FOR ANIMAL USE ONLY

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**Each gram contains:** 67 mg Trimethoprim, 333 mg Sulfadiazine

**Indications:** For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections and abscesses.

**Recommended Dose:** 3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed. Two level, loose-filled, 32cc scoops contain 37.5g, sufficient to treat 1100 lbs (500 kg) body weight. Since product contents may settle, gentle agitation during scooping is recommended.

See package insert for additional information.

#### KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

**Warning:** Do not use in horses intended for human consumption.

**Manufactured by:** Neogen Corporation Lexington, KY 40511 USA • 859-254-1221

animalsafety.neogen.com L3408-0420

Rev. 04/20

Made in the USA

Item No. AUP375

#### FOR ANIMAL USE ONLY

#### Each gram contains:

Trimethoprim 67 mg Sulfadiazine 333 mg

#### Indications:

For control of bacterial infections during treatment of acute strangles, respiratory tract infections, acute urogenital infections, wound infections, and abscesses.

#### **Recommended Dose:**

3.75 g per 110 lbs (50 kg) body weight once daily in a small amount of palatable feed.

One packet contains 37.5 g, sufficient to treat 1100 lbs (500 kg) body weight.

See package insert for additional information.

Rev. 04/20 Made in the USA



## KEEP OUT OF REACH OF CHILDREN

Store at or below 25°C (77°F)

#### Warning:

Do not use in horses intended for human consumption.



Manufactured by: Neogen Corporation
Lexington, KY 40511 USA • 859-254-1221
animalsafety.neogen.com L3408-0420



#### **UNIPRIM**

trimethoprim and sulfadiazine powder

# Product Information Product Type PRESCRIPTION ANIMAL DRUG Item Code (Source) NDC:59051-3011 Route of Administration ORAL

Active Ingredient/Active Moiety				
Ingredient Name	Basis of Strength	Strength		
Trimethoprim (UNII: AN164J8Y0X) (Trimethoprim - UNII:AN164J8Y0X)	Trime tho prim	67 mg in 1 g		
Sulfadiazine (UNII: 0N7609K889) (Sulfadiazine - UNII:0N7609K889)	Sulfadiazine	333 mg in 1 g		

Product Characteristics				
Color		Score		
Shape		Size		
Flavor	APPLE (Apple Flavored)	Imprint Code		

#### Contains

P	Packaging						
#	Item Code	Package Description	<b>Marketing Start Date</b>	Marketing End Date			
1	NDC:59051-3011-3	400 g in 1 JAR					
2	NDC:59051-3011-1	37.5 g in 1 PACKET					
3	NDC:59051-3011-4	200 g in 1 JAR					
4	NDC:59051-3011-5	1200 g in 1 JAR					
5	NDC:59051-3011-6	2000 g in 1 PAIL					

Marketing Information					
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date		
ANADA	ANADA200033	08/04/2010			

## Labeler - Neogen Corporation (042125879)

Revised: 4/2020 Neogen Corporation