

Approval Date: JUL 31 2006

FREEDOM OF INFORMATION SUMMARY

**ORIGINAL ABBREVIATED NEW ANIMAL
DRUG APPLICATION**

ANADA 200-395

**Gentamicin Sulfate Solution
(gentamicin sulfate)**

**Recommended for the control of bacterial infections of the uterus
(metritis) in horses and as an aid in improving conception in
mares with uterine infections caused by bacteria sensitive to
gentamicin**

**Sponsored by:
Sparhawk Laboratories, Inc.**

ANADA 2006-200-395

FOIS 1

Table of Contents

1.	GENERAL INFORMATION:.....	1
2.	TARGET ANIMAL SAFETY AND DRUG EFFECTIVNESS:.....	2
3.	HUMAN SAFETY:	2
4.	AGENCY CONCLUSIONS:.....	2
5.	ATTACHMENTS:	3

1. GENERAL INFORMATION:

- a. File Number: ANADA 200-395
- b. Sponsor: Sparhawk Laboratories, Inc.
12340 Santa Fe Trail Dr.
Lenexa, KS 66215
- Drug Labeler Code: 058005
- c. Established Name: Gentamicin sulfate
- d. Proprietary Name: Gentamicin sulfate solution
- e. Dosage Form: Intra-uterine injection
- f. How Supplied: 100 mL vial
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: 100 mg gentamicin sulfate/mL
- i. Route of Administration: Intra-uterine injection
- j. Species/Class: Horses
- k. Recommended Dosage: 2.0 – 2.5 grams per day for 3 to 5 days during estrus. Each dose should be diluted with 200 – 500 mL of sterile physiological saline before aseptic uterine infusion
- l. Pharmacological Category: Aminoglycoside antimicrobial
- m. Indications: Recommended for the control of bacterial infections of the uterus (metritis) in horses and as an aid in improving conceptions in mares with uterine infections caused by bacteria sensitive to gentamicin.
- n. Pioneer Product: GENTOCIN Solution Veterinary;
gentamicin sulfate; NADA 046-724;
Schering-Plough Animal Health Corp.

2. **TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:**

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor shows the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guidance, revised October 09, 2002).

Based on the formulation characteristics of the generic product Sparhawk Laboratories, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product Gentamicin Sulfate Solution. The generic product is administered as an intra-uterine injection in horses, contains the same active ingredients in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product, GENTOCIN Solution Veterinary, the subject of Schering-Plough Animal Health Corp., NADA 046-724, was approved on October 14, 1972.

3. **HUMAN SAFETY:**

This drug is intended for use in horses, which are non-food animals. Because this new animal drug is not intended for use in food-producing animals, data on human safety pertaining to drug residues in food were not required for approval of this ANADA.

Human Warnings are provided on the product label as follows: Do not use in horses intended for human consumption.

4. **AGENCY CONCLUSIONS:**

This ANADA filed under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that Gentamicin Sulfate Solution, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ***ATTACHMENTS:***

Facsimile labeling is attached as indicated below:

Generic animal drug labeling for ANADA 200-395
Gentamicin Sulfate Solution; vial label and package outsert

Pioneer animal drug labeling for NADA 046-724
GENTOCIN Solution Veterinary; vial label; container label; package insert

<p>INDICATIONS: Gentamicin Sulfate Solution is recommended for the control of bacterial infections of the uterus (metritis) in horses and as an aid in improving conception in mares with uterine infections caused by bacteria sensitive to gentamicin.</p> <p>DOSEAGE AND ADMINISTRATION: The recommended dose is 20 to 25 mL (2.0-2.5 grams) Gentamicin Sulfate Solution per day for 3 to 5 days during estrus. Each dose should be diluted with 200-500 mL of sterile physiological saline before aseptic uterine infusion.</p> <p>Read accompanying directions carefully.</p> <p>Warning: Do not use for horses intended for human consumption.</p> <p>Lot No. _____ Exp. Date _____</p>	<p align="center">GENTAMICIN SULFATE SOLUTION</p> <p align="center">Sterile Multiple Dose Vial</p> <p align="center">100 mg/mL</p> <p>Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.</p> <p>ANADA 200-986, Approved by FDA</p> <p align="center">NET CONTENTS: 100 mL</p> <p align="center">SPARHAWK LABORATORIES, INC.</p>	<p>For intra-uterine use in horses only. Each mL contains: Gentamicin sulfate veterinary equivalent to 100 mg gentamicin base; 2.4 mg sodium metabisulfite; 0.8 mg sodium sulfite, anhydrous; 0.1 mg edetate disodium; 10 mg benzyl alcohol as preservative; water for injection q.s.</p> <p>Store between 2° and 30°C (36° and 86°F). Protect from freezing.</p> <p align="center"> SEE THESE LABELS</p> <p>Manufactured by Sparhawk Laboratories, Inc. Lenexa, KS 66215, USA</p> <p align="right">G-6336-04 Rev. 12-04</p> <p align="right">Printed in U.S.A. Mfg. in U.S.A.</p>
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<p>Store between 2° and 30°C (36° and 86°F).</p> <p>REFERENCES:</p> <p>1. Harnerney, F.W., et al. <i>In vitro</i> activity of gentamicin against bacteria isolated from domestic animals. <i>Veterinary Medicine/Small Animal Clinician</i>. Nov. 1971; 1118-1122.</p> <p>2. Black, J., et al. Pharmacology of gentamicin, a new broad spectrum antibiotic. <i>Antimicrob Agents and Chemother</i>. 1963; 136-147.</p> <p align="center">7</p>	<p>For intra-uterine use in horses only. Each mL contains: Gentamicin sulfate veterinary equivalent to 100 mg gentamicin base; 2.4 mg sodium metabisulfite; 0.8 mg sodium sulfite, anhydrous; 0.1 mg edetate disodium; 10 mg benzyl alcohol as preservative; water for injection q.s.</p> <p>Store between 2° and 30°C (36° and 86°F). Protect from freezing.</p> <p align="center"> SEE THESE LABELS</p> <p>Manufactured by Sparhawk Laboratories, Inc. Lenexa, KS 66215, USA</p> <p align="right">G-6336-04 Rev. 12-04</p> <p align="right">Printed in U.S.A. Mfg. in U.S.A.</p>	<p>ANADA 200-986, Approved by FDA</p> <p align="center">GENTAMICIN SULFATE SOLUTION</p> <p align="center">100 mg/mL</p> <p align="center">For Use in Horses Only</p> <p>CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.</p> <p>DESCRIPTION: Each mL of Gentamicin sulfate veterinary equivalent to 100 mg gentamicin base; 2.4 mg sodium metabisulfite; 0.8 mg sodium sulfite, anhydrous; 0.1 mg edetate disodium; 10 mg benzyl alcohol as preservative; water for injection q.s.</p> <p>CHEMISTRY: Gentamicin is a mixture of aminoglycoside antibiotics derived from</p> <p align="center">1</p>	<p>the fermentation of <i>Micromonospora purpurea</i>. Gentamicin sulfate is a mixture of sulfate salts of the antibiotics produced in this fermentation. The salts are weakly acidic, freely soluble in water, and stable in solution.</p> <p>ANTIBACTERIAL ACTIVITY: <i>In vitro</i> antibacterial activity has shown that gentamicin is active against most gram-negative and gram-positive bacteria isolated from domestic animals.¹ Gentamicin is active against <i>Pseudomonas aeruginosa</i>, indole-positive and -negative <i>Proteus</i> species, <i>Escherichia coli</i>, <i>Klebsiella</i> species, <i>Enterobacter</i> species, <i>Alcaligenes</i> species, <i>Staphylococcus</i> species, and <i>Streptococcus</i> species.</p> <p align="center">2</p>
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<p>PHARMACOLOGY: Studies in man indicate that recommended doses of gentamicin produce a serum concentration bactericidal for most bacteria sensitive to gentamicin within an hour after intramuscular injection; these concentrations last for 8 to 12 hours.² Some 30% of the administered dose of gentamicin is bound by serum proteins and released as the drug is excreted.</p> <p>Gentamicin is excreted almost entirely by glomerular filtration. High concentrations of the active form are found in the urine. Fifty to 100% of the gentamicin injected can be recovered unchanged within 24 hours from the urine of patients with normal renal function. A small amount is excreted into the bile.</p> <p align="center">3</p>	<p>TOXICITY STUDIES: No toxic effects were observed in rats given gentamicin sulfate 20 mg/kg/day for 24 days; in cats given 10 mg/kg/day for 40 days. Gentamicin sulfate given to dogs at 6 mg/kg/day, 6 days weekly for 3 weeks, caused no detectable kidney damage. At higher doses, impairment of equilibrium and renal function were observed in these species.</p> <p>INDICATIONS: Gentamicin Sulfate Solution is recommended for the control of bacterial infections of the uterus (metritis) in horses and as an aid in improving conception in mares with uterine infections caused by bacteria sensitive to gentamicin. Bacteriologic studies should be</p> <p align="center">4</p>	<p>conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose.</p> <p>DOSEAGE AND ADMINISTRATION: The recommended dose is 20 to 25 mL (2.0 - 2.5 grams) gentamicin sulfate solution per day for 3 to 5 days during estrus. Each dose should be diluted with 200-500 mL of sterile physiological saline before aseptic uterine infusion.</p> <p>CONTRAINDICATIONS: There are no known contraindications to this drug when used as directed.</p> <p>PRECAUTION: If hypersensitivity to any of the components develops, or if overgrowth of nonsusceptible bacteria, fungi, or yeasts occurs, treatment with</p> <p align="center">5</p>	<p>Gentamicin Sulfate Solution should be discontinued and appropriate therapy instituted.</p> <p>Although Gentamicin Sulfate Solution is not sporicidal, treatment should not be given the day of breeding.</p> <p>Warning: Do not use for horses intended for human consumption.</p> <p>SIDE EFFECTS: There have been no reports of drug hypersensitivity or adverse side effects following the recommended intravaginal infusion of gentamicin sulfate solution combined with sterile physiological saline in mares.</p> <p>HOW SUPPLIED: Gentamicin Sulfate Solution, 100 mg per mL, for intra-uterine use, is available in 100 mL multiple dose vials.</p> <p align="center">6</p>
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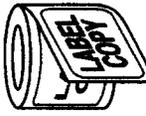
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Customer: Sparhawk / Veterinary P.O. #: Rachel CYREL #: 33928 (In)

Salesperson: Joe Bidnick - jbidnick@tabcoinc.com Customer Service: Kathy Roper - kroper@tabcoinc.com

Date 02/09/04 2/12/04 12/20/04 12/29/04 06/29/06

<p>desc.: <u>Gentamicin Sulfate Solution</u> size: <u>1.875</u> " x <u>5.75</u> "</p> <p>varnish: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No colors: <u>black</u> <u>202 red</u> <u>877 silver</u></p> <p><input type="checkbox"/> pattern _____</p> <p><input type="checkbox"/> flood _____</p>	<p align="center">Unwind #: <u>4</u></p> 
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Approved by: _____ OK as shown make corrections and resubmit OK w / corrections and resubmit Date: _____

© 1994 Schering-Plough Animal Health. All rights reserved. NADA #46-724. For information on this product, contact your veterinarian or Schering-Plough Animal Health, Kenilworth, NJ 07033.

For intra-uterine use in horses only.

Each mL contains: gentamicin sulfate, veterinary equivalent to 100 mg gentamicin base, 2.4 mg sodium metabisulfite, 0.8 mg sodium sulfite, anhydrous, 0.1 mg edetate disodium, 10 mg benzyl alcohol as preservative, water for injection q.s.

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

Protect from freezing.

Read accompanying directions carefully.

Warning: Not for use in horses intended for food.



NDC-0061-0457-03

Gentocin®
(GENTAMICIN SULFATE VETERINARY)
Solution
Veterinary

100 mg per mL
Sterile

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

NADA #46-724, Approved by FDA.

Schering-Plough Animal Health

LOT
EXP

12935552
Rev. 11/93

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Kenilworth, NJ 07033. All rights reserved.

Gentocin[®]
 (GENTAMICIN SULFATE
 VETERINARY)
 Solution
 Veterinary

Each mL contains: Gentamicin sulfate veterinary equivalent to 100 mg gentamicin base; 2.4 mg sodium metabisulfite; 0.8 mg sodium sulfite, anhydrous; 0.1 mg edetate disodium; 10 mg benzyl alcohol as preservative; water for injection q.s.

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

Protect from freezing.

Read accompanying directions carefully.

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 Schering-Plough Animal Health Corp.,
 Kenilworth, NJ 07033
 13405735 Rev. 1/92



Gentocin[®]
 (GENTAMICIN SULFATE
 VETERINARY)
 Solution
 Veterinary

Gentocin[®]
 (GENTAMICIN SULFATE
 VETERINARY)
 Solution
 Veterinary

For intra-uterine use in horses only.

Warning: Not for use in horses intended for food.



100 mg/mL

Sterile

NDC-0061-0457-03

Gentocin[®]
 (GENTAMICIN SULFATE
 VETERINARY)
 Solution
 Veterinary

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Schering-Plough
 Animal Health



Gentocin[®]
 (GENTAMICIN SULFATE
 VETERINARY)
 Solution
 Veterinary

For intra-uterine use in horses only.

Warning: Not for use in horses intended for food.



13406553

PRODUCT INFORMATION

NADA #46-724, Approved by FDA.

**GENTOCIN®
(GENTAMICIN SULFATE
VETERINARY)**

Solution 100 mg/mL

**Veterinary
For Use in Horses Only**

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

DESCRIPTION Each mL of GENTOCIN Solution contains: gentamicin sulfate veterinary equivalent to 100 mg gentamicin base; 2.4 mg sodium metabisulfite; 0.8 mg sodium sulfite, anhydrous; 0.1 mg edetate disodium; 10 mg benzyl alcohol as preservative; water for injection q.s.

CHEMISTRY Gentamicin is a mixture of aminoglycoside antibiotics derived from the fermentation of *Micromonospora purpurea*. Gentamicin sulfate veterinary is a mixture of sulfate salts of the antibiotics produced in this fermentation. The salts are weakly acidic, freely soluble in water, and stable in solution.

ANTIBACTERIAL ACTIVITY *In vitro* antibacterial activity has shown that gentamicin is active against most gram-negative and gram-positive bacteria isolated from domestic animals.¹ Gentamicin is active against *Pseudomonas aeruginosa*, indole-positive and -negative *Proteus* species, *Escherichia coli*, *Klebsiella* species, *Aerobacter* species, *Alcaligenes* species, *Staphylococcus* species, and *Streptococcus* species.

PHARMACOLOGY Studies in man indicate that recommended doses of gentamicin produce serum concentrations bactericidal for most bacteria sensitive to gentamicin within an hour after intramuscular injection; these concentrations last for 6 to 12 hours.² Some 30% of the administered dose of gentamicin is bound by serum proteins and released as the drug is excreted.

Gentamicin is excreted almost entirely by glomerular filtration. High concentrations of the active form are found in the urine. Fifty to 100% of the gentamicin injected can be recovered unchanged within 24 hours from the urine of patients with normal renal function. A small amount is excreted into the bile.

TOXICITY STUDIES No toxic effects were observed in rats given gentamicin sulfate 20 mg/kg/day for 24 days; in cats given 10 mg/kg/day for 40 days. Gentamicin sulfate given to dogs at 6 mg/lb/day, 6 days weekly for 3 weeks, caused no detectable kidney damage. At higher doses, impairment of equilib-

rium and renal function was observed in these species.

INDICATIONS GENTOCIN Solution is recommended for the control of bacterial infections of the uterus (metritis) in horses and as an aid in improving conception in mares with uterine infections caused by bacteria sensitive to gentamicin.

Bacteriologic studies should be conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose.

DOSAGE AND ADMINISTRATION The recommended dose is 20 to 25 mL (2.0-2.5 grams) GENTOCIN Solution per day for 3 to 5 days during estrus. Each dose should be diluted with 200-500 mL of sterile physiological saline before aseptic uterine infusion.

CONTRAINDICATIONS There are no known contraindications to this drug when used as directed.

PRECAUTION If hypersensitivity to any of the components develops, or if overgrowth of non-susceptible bacteria, fungi, or yeasts occurs, treatment with GENTOCIN Solution should be discontinued and appropriate therapy instituted.

Although GENTOCIN Solution is not spermicidal, treatment should not be given the day of breeding.

WARNING Not for use in horses intended for food.

SIDE EFFECTS There have been no reports of drug hypersensitivity or adverse side effects following the recommended intra-uterine infusion of GENTOCIN Solution combined with sterile physiological saline in mares.

HOW SUPPLIED GENTOCIN Solution, 100 mg per mL for intrauterine use is available in 100 mL and 250 mL multiple-dose vials.

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

Protect from freezing.

REFERENCES

1. Hennessey PW, et al. *In vitro* activity of gentamicin against bacteria isolated from domestic animals. *Veterinary Medicine/Small Animal Clinician*. Nov. 1971;1118-1122.
2. Black J, et al. Pharmacology of gentamicin, a new broad spectrum antibiotic. *Antimicrob Agents and Chemother*. 1963; 138-147.

September 1995

Schering-Plough Animal Health Corp.
Kenilworth, NJ 07033

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