

JUL 3 2000

FREEDOM OF INFORMATION (FOI) SUMMARY

NEORAL (neomycin oral solution)

ANADA 200-289

Med-Pharmex, Inc.

2727 Thompson Creek Road

Pomona, CA 91767-1861

Date of Approval _____

ANADA 200-289

FOIS 1

FREEDOM OF INFORMATION SUMMARY

- I. GENERAL INFORMATION: ANADA 200-289
- ANADA Sponsor:
Med-Pharmex, Inc.
2727 Thompson Creek Road
Pomona, CA 91767-1861
- A. Established Name: neomycin sulfate
- B. Trade/Proprietary Name: Neoral Oral Solution
- C. Dosage Form: oral solution
- D. How Supplied: 473.1 mL (1 Pt), 3.785 L (1 Gal)
- E. How Dispensed: OTC
- F. Amount of Active Ingredients: 200 mg of neomycin sulfate per mL (140 mg neomycin base per mL).
- G. Route of Administration: Orally in drinking water or milk
- H. Species: Cattle (excluding veal calves), Swine, Sheep, and Goats.
- I. Labeled Dosage: Administer to cattle (excluding veal calves), swine, sheep, and goats at a dose of 10 mg neomycin sulfate per pound of body weight in divided doses for a maximum of 14 days.
- J. Pharmacological Category: Antibiotic
- K. Indications for Use: For the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin sulfate.
- L. Pioneer/NADA #: Pharmacia & Upjohn Company, Neomix® 325, NADA 011-315

II. 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, (53 FR 50460, December 15, 1988, First GADPTRA Policy Letter) 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 data, drug effectiveness data, and human food safety data (other than tissue residue data) are not required for approval of an ANADA. An ANADA relies on the target animal safety, drug effectiveness, and human food safety data in the pioneer's new animal drug application. The ANADA sponsor is required to show that the generic product is bioequivalent to the pioneer. ANADA's for drug products for food-producing animals will generally be required to include bioequivalence and tissue residue studies. A tissue residue study will generally be required to accompany clinical end-point and pharmacologic end-point bioequivalence studies, and blood level bioequivalence studies that can not quantify the concentration of the drug in blood throughout the established withdrawal period. For certain dosage forms, the agency will grant a waiver from conducting an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, April 1990).

An oral solution as a generic copy of a soluble powder is a change in dosage form that is permissible under the GADPTRA. On October 1, 1992, a suitability petition (92P-0363/CP1) was approved to allow a generic sponsor (Phoenix Scientific, Inc.) to file an ANADA for a neomycin oral solution as a generic copy of the pioneer (Pharmacia & Upjohn) neomycin sulfate soluble powder, Neomix® 325, NADA 11-315. Relying on the conclusions of suitability petition (92P-0363/CP1), Med-Pharmex's generic product is approved as a copy of the pioneer product sponsored by Pharmacia & Upjohn Company.

Based upon the formulation characteristics of the generic product, Med-Pharmex was granted a waiver from conducting an *in vivo* bioequivalence study for neomycin sulfate. The generic and pioneer products contain the same active ingredient, and no differences in the inactive ingredients which would affect bioavailability of the active ingredient. The pioneer and generic products are administered as oral solutions.

The generic product is formulated as a solution, and the pioneer product is formulated as a water soluble powder. The generic product is formulated at 200 mg neomycin sulfate/mL, and the pioneer product is formulated at 325 g neomycin sulfate/pound of product. The pioneer and generic products will be administered as oral solutions in water or milk, at a dosage of 10 mg neomycin sulfate per pound body weight in divided doses for a maximum of 14 days.

III. HUMAN FOOD SAFETY

Tolerance

A tolerance of 7.2 parts per million (ppm) is established for residues of parent neomycin (marker residue) uncooked edible kidney (target tissue 7.2 ppm in fat, 3.6 ppm in liver, 1.2 ppm in muscle of cattle, swine, sheep, and goats. A tolerance of 0.15 ppm is established for neomycin in milk (21 CFR 556.430).

Withdrawal Period

When a waiver of *in vivo* bioequivalence testing is granted, the withdrawal times are those previously assigned to the pioneer product.

The withdrawal times are 1 day for cattle, 3 days for swine and goats, and 2 days for sheep.

Regulatory Method for Residues

The regulatory analytical method for detection of residues of the drug is a microbiological test using *Staphylococcus epidermidis* suspension. The method is published by the Food and Drug Administration, "Antibiotic Residues in Milk, Dairy Products and Animal Tissues: Methods, Reports, and Protocols", revised October 1968, reprinted December 1974.

IV. AGENCY CONCLUSIONS

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that neomycin sulfate oral solution when used under the proposed conditions of use, is safe and effective for its labeled indications.

Attachments: The following generic labeling and currently approved pioneer labeling are attached.

1. Facsimile package label for Neoral Oral Solution for 473.1 mL (1 Pt), and 3.785 L (1 Gal).
2. Approved pioneer package label for neomycin sulfate - Neomycin 325 Soluble Powder for 3.5 oz packages and 50 LB bags.

DRAFT LABEL: 1 PINT

Restricted Drug - Use Only As Directed (California)

INDICATIONS: For the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin sulfate in cattle (excluding veal calves), swine, sheep and goats.

DOSAGE AND

ADMINISTRATION: Administer to cattle (excluding veal calves), swine, sheep and goats at a dose of 10 mg neomycin sulfate per pound of body weight in divided doses for a maximum of 14 days.

Dosage Schedule for treatment of colibacillosis

<u>Pounds of Body Weight</u>	<u>Amount of Neomycin Oral Solution Per Day in Divided Doses</u>
25 lbs	1.2 mL (1/4 teaspoonful)
50 lbs	2.5 mL (1/2 teaspoonful)
100 lbs	5.0 mL (1 teaspoonful)
300 lbs	15 mL (1 tablespoonful)
591.5 lbs	29.5 mL (1 fluid ounce)

Teaspoon = U.S. Standard Measure.

Neomycin Oral Solution may be given undiluted or diluted with water.

Herd Treatment: Each 473 mL (1 Pt) will treat 9464 pounds of body weight. Therefore estimate the total number of pounds of body weight of the animals to be treated and administer 29.5 mL (1 Fl. Oz) for each 591.5 lbs. The product should be added to the amount of drinking water estimated to be consumed in 12-24 hours. Provide medicated water as the sole source of water each day until consumed, followed by non-medicated water as required. Fresh medicated water should be prepared each day.

Individual Animal Treatment: To provide 10 mg neomycin sulfate per pound of body weight, mix 5 mL (1 tsp) in water or milk for each 100 lbs of body weight. Administer daily either as a drench in divided dosages or in the drinking water to be consumed in 12-24 hours.

NEORAL

(NEOMYCIN ORAL SOLUTION)

ANTIBACTERIAL FOR ORAL USE ONLY

FOR ANIMAL USE ONLY

KEEP OUT OF REACH OF CHILDREN.

ANADA # 200-289

Approved by FDA

NET CONTENTS:

473 mL (1 Pt)

Med-Pharmex, Inc.
Pomona, CA 91767-1861

COMPOSITION: Each mL contains 200 mg of Neomycin Sulfate equivalent to 140 mg of neomycin base.

CAUTION: To administer the stated dosage, the concentration of neomycin required in medicated water must be adjusted to compensate for variation in age and weight of animal, the nature and severity of disease signs, and environmental temperature and humidity, each of which affects water consumption.

If symptoms persist after using this preparation for 2 or 3 days, consult a veterinarian. If symptoms such as fever, depression or going off feed develop, oral neomycin is not indicated as the sole treatment since systemic levels of neomycin are not obtained due to poor absorption from the gastrointestinal tract.

Important: Treatment should continue 24 to 48 hours beyond remission of disease symptoms, but not to exceed a total of 14 consecutive days. Animals not drinking or eating should be treated individually by drench.

WARNING: Discontinue treatment prior to slaughter as follows:

Cattle - 1 day
Sheep - 2 days
Swine and goats - 3 days

Store at controlled room temperature 15°C to 30°C (59°F to 86°F).

Lot No / Exp. Date.

DRAFT LABEL: 1 Gallon:

Restricted Drug - Use Only As Directed (California)

INDICATIONS: For the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin sulfate in cattle (excluding veal calves), swine, sheep and goats.

DOSAGE AND

ADMINISTRATION: Administer to cattle (excluding veal calves), swine, sheep and goats at a dose of 10 mg neomycin sulfate per pound of body weight in divided doses for a maximum of 14 days.

Dosage Schedule for treatment of colibacillosis

Pounds of <u>Body Weight</u>	Amount of Neomycin Oral Solution Per Day <u>in Divided Doses</u>
25 lbs	1.2 mL (1/4 teaspoonful)
50 lbs	2.5 mL (1/2 teaspoonful)
100 lbs	5.0 mL (1 teaspoonful)
300 lbs	15 mL (1 tablespoonful)
591.5 lbs	29.5 mL (1 fluid ounce)

Teaspoon = U.S. Standard Measure.

Neomycin Oral Solution may be given undiluted or diluted with water.

Herd Treatment: Each 473 mL (1 Pt) will treat 9464 pounds of body weight. Therefore estimate the total number of pounds of body weight of the animals to be treated and administer 29.5 mL (1 Fl. Oz) for each 591.5 lbs. The product should be added to the amount of drinking water estimated to be consumed in 12-24 hours. Provide medicated water as the sole source of water each day until consumed, followed by non-medicated water as required. Fresh medicated water should be prepared each day.

Individual Animal Treatment: To provide 10 mg neomycin sulfate per pound of body weight, mix 5 mL (1 tsp) in water or milk for each 100 lbs of body weight. Administer daily either as a drench in divided dosages or in the drinking water to be consumed in 12-24 hours.

NEORAL

(NEOMYCIN ORAL
SOLUTION)

ANTIBACTERIAL
FOR ORAL USE ONLY

FOR ANIMAL USE ONLY

KEEP OUT OF REACH OF
CHILDREN.

ANADA # 200-289

Approved by FDA

NET CONTENTS:

3.785 Liters (1 GALLON)

Med-Pharmex, Inc.
Pomona, CA 91767-1861

COMPOSITION: Each mL contains 200 mg of Neomycin Sulfate equivalent to 140 mg of neomycin base.

CAUTION: To administer the stated dosage, the concentration of neomycin required in medicated water must be adjusted to compensate for variation in age and weight of animal, the nature and severity of disease signs, and environmental temperature and humidity, each of which affects water consumption.

If symptoms persist after using this preparation for 2 or 3 days, consult a veterinarian. If symptoms such as fever, depression or going off feed develop, oral neomycin is not indicated as the sole treatment since systemic levels of neomycin are not obtained due to poor absorption from the gastrointestinal tract.

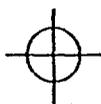
Important: Treatment should continue 24 to 48 hours beyond remission of disease symptoms, but not to exceed a total of 14 consecutive days. Animals not drinking or eating should be treated individually by drench.

WARNING: Discontinue treatment prior to slaughter as follows:

Cattle – 1 day
Sheep – 2 days
Swine and goats - 3 days

Store at controlled room temperature
15°C to 30°C (59°F to 86°F).

Lot No / Exp. Date.



NDC 0009-0553-40

Neomix[®] 325

Soluble Powder

neomycin sulfate (commercial grade)



Antibacterial



For the treatment and control of colibacillosis (Bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin sulfate in cattle, swine, sheep and goats.

For the control of mortality associated with *Escherichia coli* organisms susceptible to neomycin sulfate in growing turkeys.

Each Packet Contains:

7.15 gm neomycin sulfate (commercial grade)
equivalent to 50 gm neomycin

NADA #11-312 Approved by FDA

Restricted Drug—Use Only As Directed (California)

Pharmacia
& Upjohn

NET WT 3.5 Oz (100 Grams)

ADDITIONAL INFORMATION				
SIZE	5 X 7	IMPRINT SIZE	X	DRAWING #
PRODUCT	NEOMIX 325 Foil	CCS #	553-40	EOP #
COMPOSITION ORDER #	4745	COPY CODE #	813 860 006D	DATE
TYPESET BY	L. Amos	BOTTLE #	X	3/24/99



Pharmacia & Upjohn
Composition Unit 2566

For Use in Animals Only **Store at room temperature**
Add to drinking water—Not for use in liquid supplements

Dosage and Administration: Administer to turkeys at a dose of 10 mg neomycin sulfate per pound of body weight per day for a maximum of 5 days. Administer to cattle, swine, sheep and goats at a dose of 10 mg neomycin sulfate per pound of body weight per day in divided doses for a maximum of 14 days.

Herd/Flock Treatment: Each packet will treat 7150 pounds body weight. Therefore, estimate the total number of pounds of body weight of the animals to be treated and administer one (1) packet (or portion thereof) for each 7150 pounds. The product should be added to the amount of drinking water estimated to be consumed in 12-24 hours. Provide medicated water as the sole source of water each day until consumed, followed by non-medicated water as required. Fresh medicated water should be prepared each day.

Individual Animal Treatment: To provide 10 mg neomycin sulfate per pound of body weight, mix one (1) level teaspoon in water or milk for each 160 pounds body weight. Administer daily either as a drench in divided doses or in the drinking water to be consumed in 12-24 hours.

Drinking Water: Use the number of packets indicated below in 256 gallons of water, or in two gallons of stock solution used in proportioners set to meter one ounce per gallon.

- Swine:**
- Pigs Weighing 25 to 50 Pounds 2 Packets
 - Pigs Weighing 50 to 100 Pounds 3 Packets
 - Pigs Weighing Over 100 Pounds 4 Packets

Caution: To administer the stated dosage, the concentration of neomycin required in medicated water must be adjusted to compensate for variation in age and weight of animal, the nature and severity of disease signs, and environmental temperature and humidity, each of which affects water consumption.

If symptoms persist after using this preparation for 2 or 3 days, consult a veterinarian. If symptoms such as fever, depression, or going off feed develop, oral neomycin is not indicated as the sole treatment since systemic levels of neomycin are not obtained due to low absorption from the gastrointestinal tract.

Important: Treatment should continue 24 to 48 hours beyond remission of disease symptoms, but not to exceed a total of 14 consecutive days for cattle, swine, sheep, goats, and 5 days for turkeys. Animals not drinking or eating should be treated individually by drench.

Warning: Not for human use. Keep out of reach of children. Discontinue treatment prior to slaughter by at least the number of days listed below for the appropriate species:

- Turkeys 0 days
- Cattle 1 day
- Sheep 2 days
- Swine and goats 3 days

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal. A milk discard period has not been established for this product in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older.

3.5 OZ PACKET

0009-0553-40 1

PURCHASE SEAL

813 860 006D
 Pharmacia & Upjohn Company
 Kalamazoo, MI 49001, USA

NDC 0009-0799-04

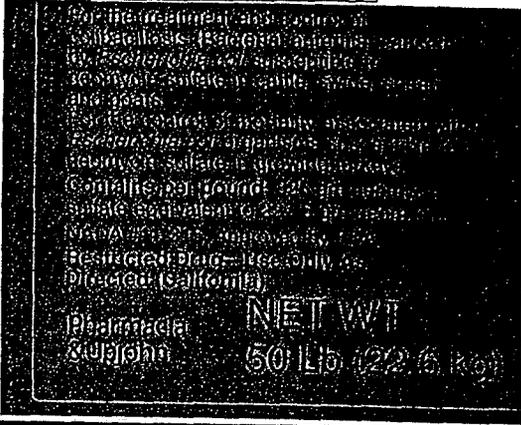
Neomix[®] AG 325 Soluble Powder

neomycin sulfate
(agricultural grade)
Antibacterial

TAKE TIME



OBSERVE LABEL
DIRECTIONS



For Use in Animals Only — Keep Container Tightly Closed — Store at Room Temperature
Add to drinking water.—Not for use in liquid supplements
Dosage and Administration: Administer 10 mg neomycin sulfate per pound of body weight
per day in divided doses for a maximum of 14 days for cattle, swine, sheep, goats, and 5 days for
turkeys.
Using measuring spoons, the recommended dosage can be determined as follows:

Daily Schedule for Drinking Water

Swine		Cattle		Turkey	
One tablespoonful* of NEOMIX AG 325 added to water consumed in one day will treat	Weight of each pig	One tablespoonful* of NEOMIX AG 325 added to water or milk consumed in one day will treat	Weight of each calf	One tablespoonful* of NEOMIX AG 325 added to water consumed in one day will treat	Weight of each bird
50 pigs	10 pounds	10 calves	50 pounds	1000 birds	.5 pound
20 pigs	25 pounds	7 calves	75 pounds	500 birds	1 pound
10 pigs	50 pounds	4 calves	125 pounds	100 birds	5 pounds
				50 birds	10 pounds

*Level Tablespoonful = US Standard Measure

The product should be added to the amount of drinking water estimated to be consumed in 12-24
hours. Provide medicated water as the sole source of water each day until consumed, followed by non-
medicated water as required. Fresh medicated water should be prepared each day. For a Stock
Solution, add six level tablespoonfuls to one gallon of water. Each pint of this stock solution will
medicate 5 gallons of drinking water.

For use in Automatic Proportioners delivering 2 ounces of stock solution per gallon of drinking
water, dissolve 9 level tablespoonfuls in a gallon of water to make the stock solution.
Individual Animal Treatment—To provide 10 mg neomycin sulfate per pound of body weight, mix
one (1) level teaspoon in water or milk for each 150 pounds of body weight. Administer daily either as
a drench in divided doses or in the drinking water to be consumed in 12-24 hours.

Caution: To administer the stated dosage, the concentration of neomycin required in medicated
water must be adjusted to compensate for variation in age and weight of animal, the nature and
severity of disease signs, and environmental temperature and humidity, each of which affects water
consumption. If symptoms persist after using this preparation for 2 or 3 days, consult a veteri-
narian. If symptoms such as fever, depression or going off feed develop, oral neomycin is not
indicated as the sole treatment since systemic levels of neomycin are not obtained due to low
absorption from the gastrointestinal tract.

Important: Treatment should continue 24 to 48 hours beyond remission of disease symptoms, but
not to exceed a total of 14 consecutive days for cattle, swine, sheep, goats, and 5 days for turkeys.
Animals not drinking or eating should be treated individually by drench.

Warning: Not for human use. Keep out of reach of children. Discontinue treatment prior
to slaughter by at least the number of days listed below for the appropriate species:

Turkeys 0 days Sheep 2 days

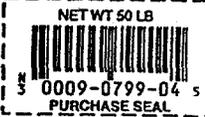
Cattle 1 day Swine and goats 3 days

A withdrawal period has not been established for this product in pre-ruminating calves.

Do not use in calves to be processed for veal.

A milk discard period has not been established for this product in lactating dairy cattle.

Do not use in female dairy cattle 20 months of age or older.



Important: Store in a dry place. When storing partially used
containers, securely close bags to prevent contents from
caking.

813 275 209D

Pharmacia & Upjohn Company
Kalamazoo, MI 49001, USA

Pharmacia & Upjohn

Composition Unit 2566

Black PMS 2915 Red 052

PRODUCT NEOMIX AG 325	COLL # 799-04	TOP # 692017	COMP CODE # 813 275 209D	COMPOSITION ORDER # 4743
SIZE 8.75x7.125	IMPRINT MARK X	DRUM/BOX # PD1480	DATE 3/24/99	PREPARED BY L. Amos
ADDITIONAL INFORMATION VARNISH ALL				