

Approval Date: JUN 14 2006

FREEDOM OF INFORMATION SUMMARY
ORIGINAL ABBREVIATED NEW ANIMAL DRUG
APPLICATION
ANADA 200-283

VETRO-MAX Ointment
(gentamicin sulfate, USP, betamethasone valerate, USP, and
clotrimazole, USP)

For the treatment of canine acute and chronic otitis externa
associated with yeast (*Malassezia pachydermatis*, formerly
***Pityrosporum canis*) and/or bacteria susceptible to gentamicin**

Sponsored by:

Altana Inc.

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

- a. File Number: ANADA 200-283
- b. Sponsor: Altana Inc.
60 Baylis Road
Melville, NY 11747

Drug Labeler Code: 025463
- c. Established Name: Gentamicin sulfate, USP, betamethasone valerate, USP, and clotrimazole, USP
- d. Proprietary Name: VETRO-MAX
- e. Dosage Form: Ointment
- f. How Supplied: 7.5-gram and 15-gram tubes
and 215-gram plastic bottles
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: Each gram contains gentamicin sulfate, USP equivalent to 3 mg gentamicin base; betamethasone valerate, USP equivalent to 1 mg betamethasone; and 10 mg clotrimazole, USP in a mineral oil-based system.
- i. Route of Administration: Topical
- j. Species/Class: Dogs
- k. Recommended Dosage: Instill 4 drops from the 7.5 g and 15 g tubes (2 drops from the 215 g bottle) twice daily into the ear canal of dogs weighing less than 30 lbs. Instill 8 drops from the 7.5 g and 15 g tubes (4 drops from the 215 g bottle) twice daily into the ear canal of dogs weighing 30 lbs. or more.
- l. Pharmacological Category: Antibiotic, anti-inflammatory, anti-pruritic, and antifungal

- m. Indications: For the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis*, formerly *Pityrosporum canis*) and/or bacteria susceptible to gentamicin.
- n. Pioneer Product: OTOMAX; gentamicin sulfate, USP, betamethasone valerate, USP, and clotrimazole, USP; NADA 140-896; 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 that 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 Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Altana Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product VETRO-MAX (gentamicin sulfate, USP, betamethasone valerate, USP, and clotrimazole, USP) Ointment. The generic product is administered as an ointment, 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, OTOMAX (gentamicin sulfate, USP, betamethasone valerate, USP, and clotrimazole, USP) Ointment, the subject of Schering-Plough Animal Health Corp's. NADA 140-896, was approved on June 9, 1993.

3. **HUMAN SAFETY:**

This drug is intended for use in dogs, 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: **“Keep Out of Reach of Children”** and **“For otic use in dogs only”**.

4. **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 VETRO-MAX Ointment, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. **ATTACHMENTS:**

Facsimile generic labeling and currently approved pioneer labeling are attached as follows:

Generic Labeling for ANADA 200-283:

VETRO-MAX Ointment

7.5 g tube

7.5 g carton

15 g tube label

15 g carton

215 g bottle label

215 g carton

Package Insert

Pioneer Labeling for NADA 140-896:

OTOMAX Ointment

7.5 g tube label

15 g tube label

15 g carton

215 g bottle label

Package Insert

Increase UPC bar height when artwork allow.
 Max. height .625", Min. height .312"

100%

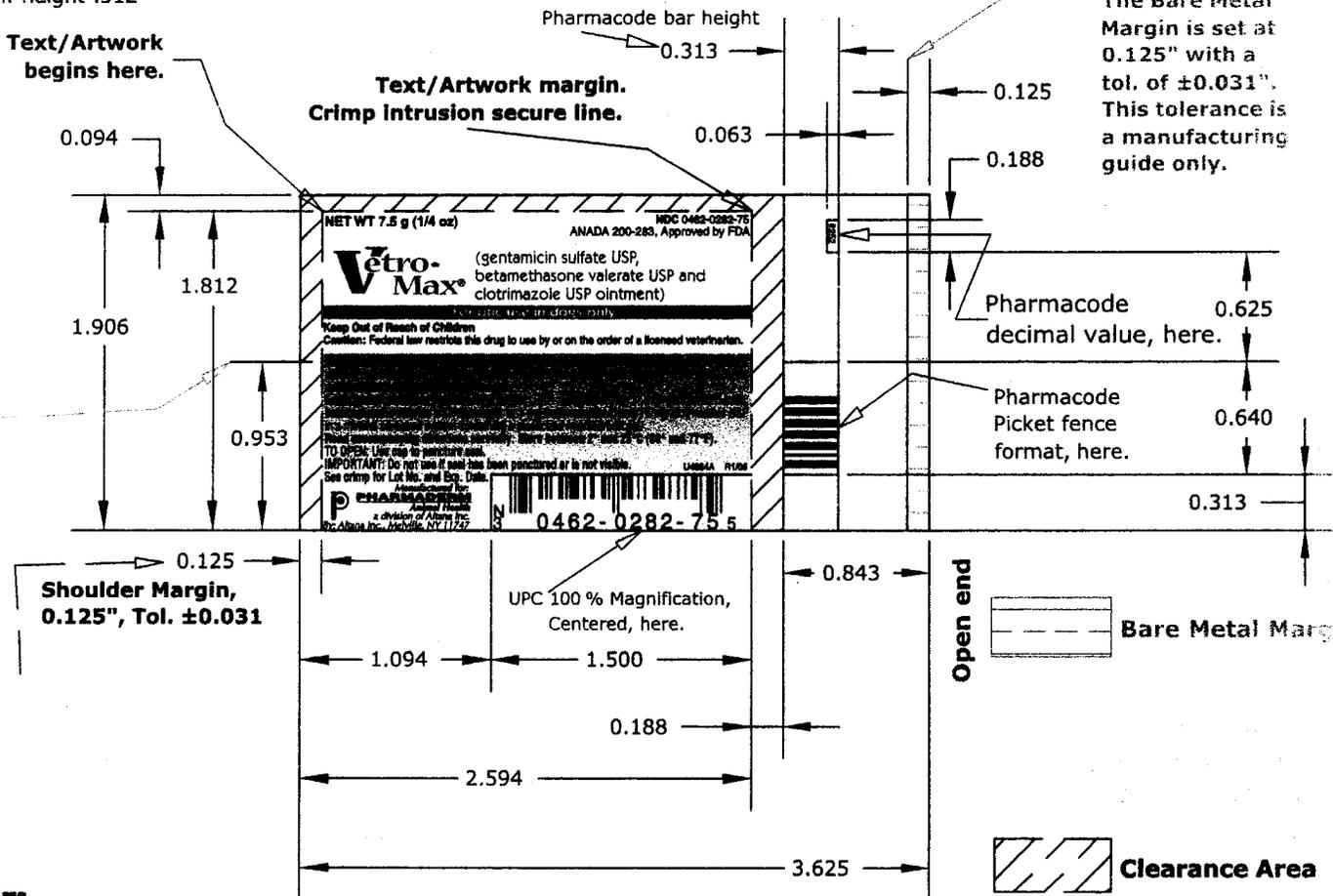
Text/Artwork begins here.

Text/Artwork margin.
 Crimp intrusion secure line.

The Bare Metal Margin is set at 0.125" with a tol. of ± 0.031 ". This tolerance is a manufacturing guide only.

Center Line.
 Front panel colors and art design may bleed over clearance areas, but no fonts allowed over clearance lines.

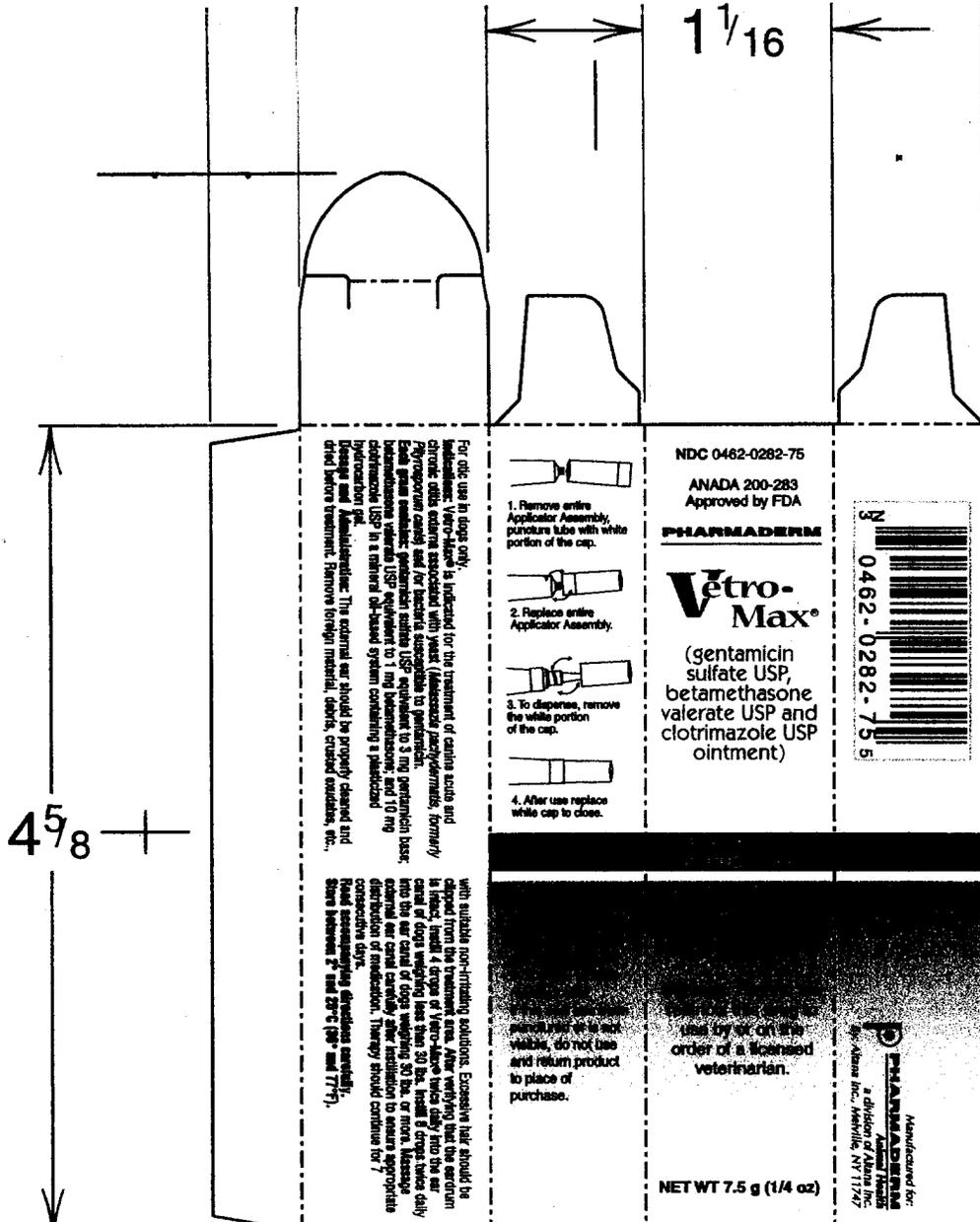
Any color/art design bleed on back panel clearance areas must fade out or end before UPC code. Likewise, no fonts over clearance lines on back panel.



Item: Vetro-max 7.5g
 Item #: U4884A SST213C
 PMS: 1795, Black, PMS 410

ALTANA Inc			5" Dia. X 3 5/8" Metal Tube, Art Base Template		
TOLERANCES		MATERIAL:			
FRACTION	DECIMAL	ANGLE	SCALE: 1:1	DRAWN BY: J. Scott	APPROVED BY:
±	±	±		DATE: 8/13/03	DATE:
					DRAWING #: AD44JWS

Revised logo address DH 8/04
 Revised and changes typeface for consistency 1/06
 Removed "veterinary" from drug name 3/06
 Removed Commas before USP 4/06



4 5/8

1 1/16

NDC 0462-0282-75
ANADA 200-283
Approved by FDA

PHARMADERM
Vetro-Max®
(gentamicin sulfate USP, betamethasone valerate USP and clotrimazole USP ointment)



1. Remove entire Applicator Assembly, puncture tube with white portion of the cap.
2. Replace entire Applicator Assembly.
3. To dispense, remove the white portion of the cap.
4. After use replace white cap to close.

Forotic use in dogs only.
Indicated for the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis*, formerly *Pityrosporum canis*) and/or bacteria susceptible to gentamicin. Each gram contains gentamicin sulfate USP equivalent to 3 mg gentamicin base, betamethasone valerate USP equivalent to 1 mg betamethasone, and 10 mg clotrimazole USP in a refined oil-based system containing a plasticized hyperacrylate gel.
Warnings: **Caution:** The external ear should be properly cleaned and dried before treatment. Remove foreign material, debris, crusted exudates, etc.

with suitable non-irritating solutions. Excessive hair should be clipped from the treatment area. After verifying that the ear drum is intact, instill 4 drops of Vetro-Max twice daily into the ear canal of dogs weighing less than 50 lbs, instill 8 drops twice daily into the ear canal of dogs weighing 50 lbs. or more. Massage ointment into ear canal carefully after attention to ensure appropriate distribution of medication. Therapy should continue for 7 consecutive days.
Keep away from children. Contains gentamicin sulfate USP, betamethasone valerate USP and clotrimazole USP (see USP 1771).

Do not use if not sterile, do not use and return product to place of purchase.

Use by or on the order of a licensed veterinarian.

NET WT 7.5 g (1/4 oz)

Manufactured for:
Pharmaderm Animal Health
a division of Alkermes Inc.
New York, NY 11747

IU4884A
#252
R1/06



252

ALTANA, INC.
DIFLORASONE 15 gr CTN.
1 1/16 x 7/8 x 4 5/8
HOWELL DESIGN No. 2498E1A1A
TEMPLATE No. 6807

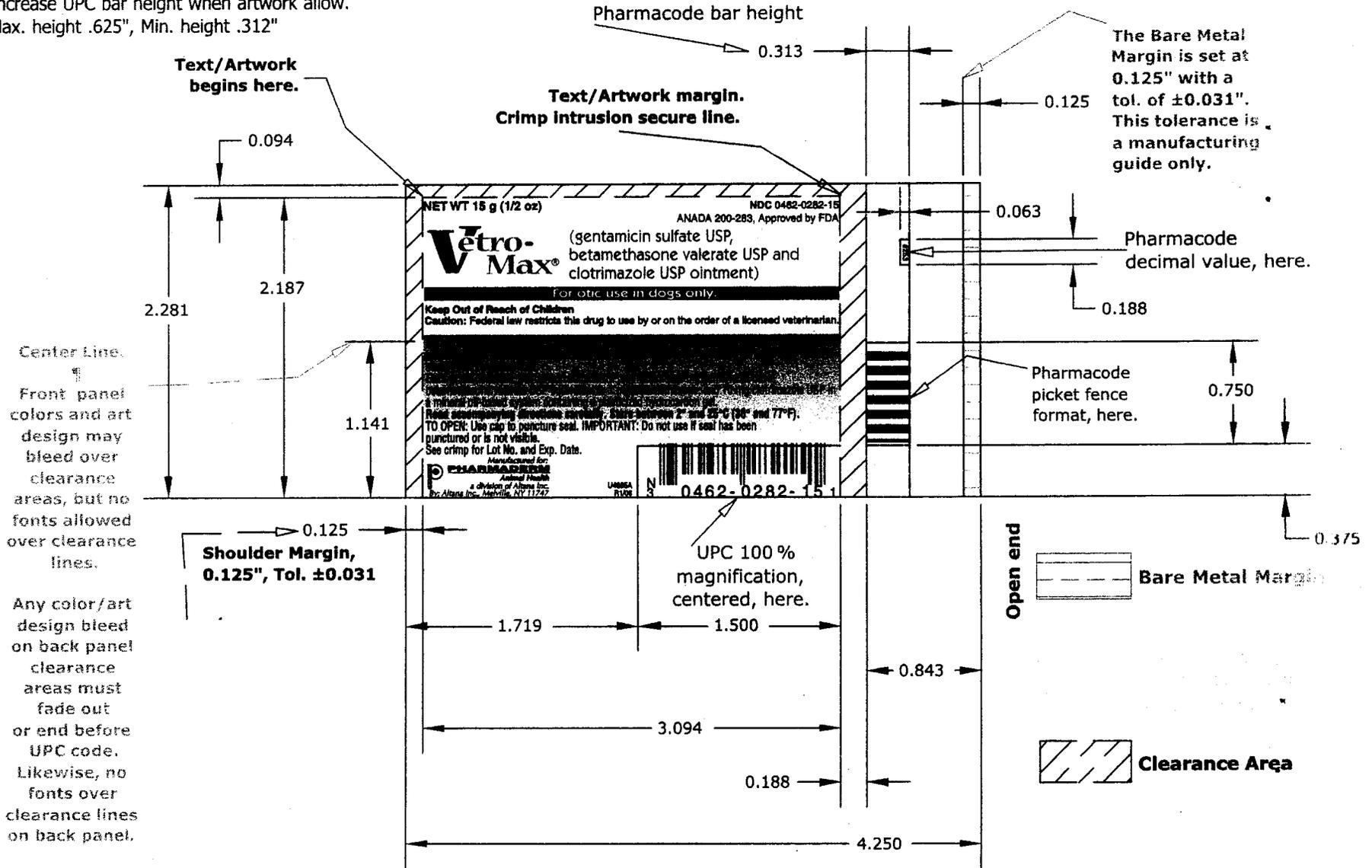
WARNING!
DO NOT MODIFY DIE LINE

PRINT SIDE

Die Size change for New Nozzel Tube - AA 10/19/00
Change color-Revised Net Wt Statement DH1/02
revised logo address DH 8/04
Increased size of text per Dr. Schaefer R10/04
Revised and changed typeface for consistency DH1/06
Removed "veterinary" from drug name 3/06
Removed commas from before USP 4/06

Text 7 on 7
IU4884A R1/06SSC-50
Dimensions: 1 1/16 x 7/8 x 4 5/8
Colors: PMS 1795, PMS 410, Black

Increase UPC bar height when artwork allow.
Max. height .625", Min. height .312"



Center Line.
Front panel colors and art design may bleed over clearance areas, but no fonts allowed over clearance lines.

Any color/art design bleed on back panel clearance areas must fade out or end before UPC code. Likewise, no fonts over clearance lines on back panel.

Text 6.5 on 6.25

Item: Vetro-max
Item #: U4885A SST28
PMS: 1795, Black, PMS 410

1/06 corrected typo in veterinary

Revised logo address DH 8/04
Adjusted and changed typeface for consistency 1/06
Removed "veterinary" from drug name 3/06

ALTANA Inc			3/4" Dia. X 4 1/4" Metal Tube, Art Base Template		
TOLERANCES		MATERIAL:			
FRACTION	DECIMAL	ANGLE	SCALE: 1:1	DRAWN BY: J. Scott	APPROVED BY:
±	±	±		REVISION DATE: 8/22/03	DATE:
				DRAWING #: AD7JWS.03	

CS

T7420

WARNING!

PRINT SIDE SHOWN

4

GRAM CTN

DO NOT MODIFY DIE LINE

3 x 1 x 5.4375(ext 1/8th inch)

For otic use in dogs only.

Indications:
Vetro-Max® is indicated for the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis*, formerly *Phytophthora canis*) and/or bacteria susceptible to gentamicin.

Each gram contains:
gentamicin sulfate USP equivalent to 3 mg gentamicin base; betamethasone valerate USP equivalent to 1 mg betamethasone; and 10 mg clotrimazole USP in a mineral oil-based system containing a plasticized hydrocarbon gel.

Dosage and Administration:
The external ear should be properly cleaned and dried before treatment. Remove foreign material, debris, crusts, exudates, etc., with suitable non-irritating solutions. Excessive hair should be clipped from the treatment area. After verifying that the eardrum is intact, instill 4 drops of Vetro-Max® twice daily into the ear canal of dogs weighing less than 30 lbs. Instill 8 drops twice daily into the ear canal of dogs weighing 30 lbs. or more. Massage external ear canal carefully after instillation to ensure appropriate distribution of medication. Therapy should continue for 7 consecutive days.

Keep accompanying directions carefully. Store between 2° and 25°C (36° and 77°F).

Manufactured for:
Pharmacia Animal Health
a division of **Alkerm Inc.**
By: Alkerm Inc., Melville, NY 11747

NDC 0462-0282-15
ANADA 200-283
Approved by FDA

PHARMACIA

Vetro-Max®
(gentamicin sulfate USP, betamethasone valerate USP and clotrimazole USP ointment)

NET WT 15 g (1/2 oz)

ILU4885A
#253
R1/06

253

Text 7 on 7
ILU4885A R1/06
SSC-7
Dimensions: 1.219" x 1.00" x 5.438"
Colors: PMS 1795, PMS 410, Black

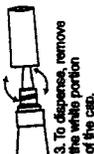
Die Size change for New Nozzel Tube-AA 10/19/00
Changed colors:
Revised Net WT statement DH 1/02
Logo address DH B/04
Increased text size per Dr.Schaefer 10/04
Removed "veterinary" from drug name 3/06
Removed commas before USP 4/06



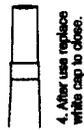
1. Remove entire Applicator Assembly, puncture tube with white portion of the cap.



2. Replace entire Applicator Assembly.



3. To dispense, remove the white portion of the cap.



4. After use replace white cap to close.

10% grey represents
unvarnished area
NOT TO PRINT



LOT NO
EXP DATE

For otic use in dogs only.
Indications: Vetro-Max[®] is indicated for the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis*, formerly *Pityrosporum canis*) and/or bacteria susceptible to gentamicin.

Each gram contains: gentamicin sulfate USP equivalent to 3 mg gentamicin base; betamethasone valerate USP equivalent to 1 mg betamethasone; and 10 mg clotrimazole USP in a mineral oil-based system containing a plasticized hydrocarbon gel.

Dosage and Administration: The external ear should be properly cleaned and dried before treatment. Remove foreign material, debris, crusted exudates, etc., with suitable non-irritating solutions. Excessive hair should be clipped from the treatment area. After verifying that the eardrum is intact, instill 2 drops of Vetro-Max[®] twice daily into the ear canal of dogs weighing less than 30 lbs. Instill 4 drops twice daily into the ear canal of dogs weighing 30 lbs. or more. Massage external ear canal carefully after instillation to ensure appropriate distribution of medication. Therapy should continue for 7 consecutive days.

Read accompanying directions carefully. Store between 2° and 25°C (36° and 77°F).

L128224A
R1/06

Manufactured for:
PHARMADERM
Animal Health
a division of Alkermes Inc.
By: Alkermes Inc., Melville, NY 11747

NDC 0462-0282-24
ANADA 200-283, Approved by FDA

PHARMADERM

**Vetro-
Max[®]**

(gentamicin sulfate USP,
betamethasone valerate
USP and clotrimazole USP
ointment)

For otic use in dogs only.

Use only as directed and only on the order of a licensed veterinarian.
Shake well before use.

NET WT 215 g (7 1/2 oz)



3 0462-0282-24 3

Item: Vetro-max
Item #: L128224A
Die Size: 6.0 x 3.5
PMS: 1795, Black, PMS 410

Corrected placement of veterinary and USP 10/04
Revised and changed type face for consistency 1/06
Removed "veterinary" from drug name 3/06
removed compass before USP 4/06

Mid-York Press Inc

job# 15033 8/3/05

Altana

Animax w/sthuhl cap

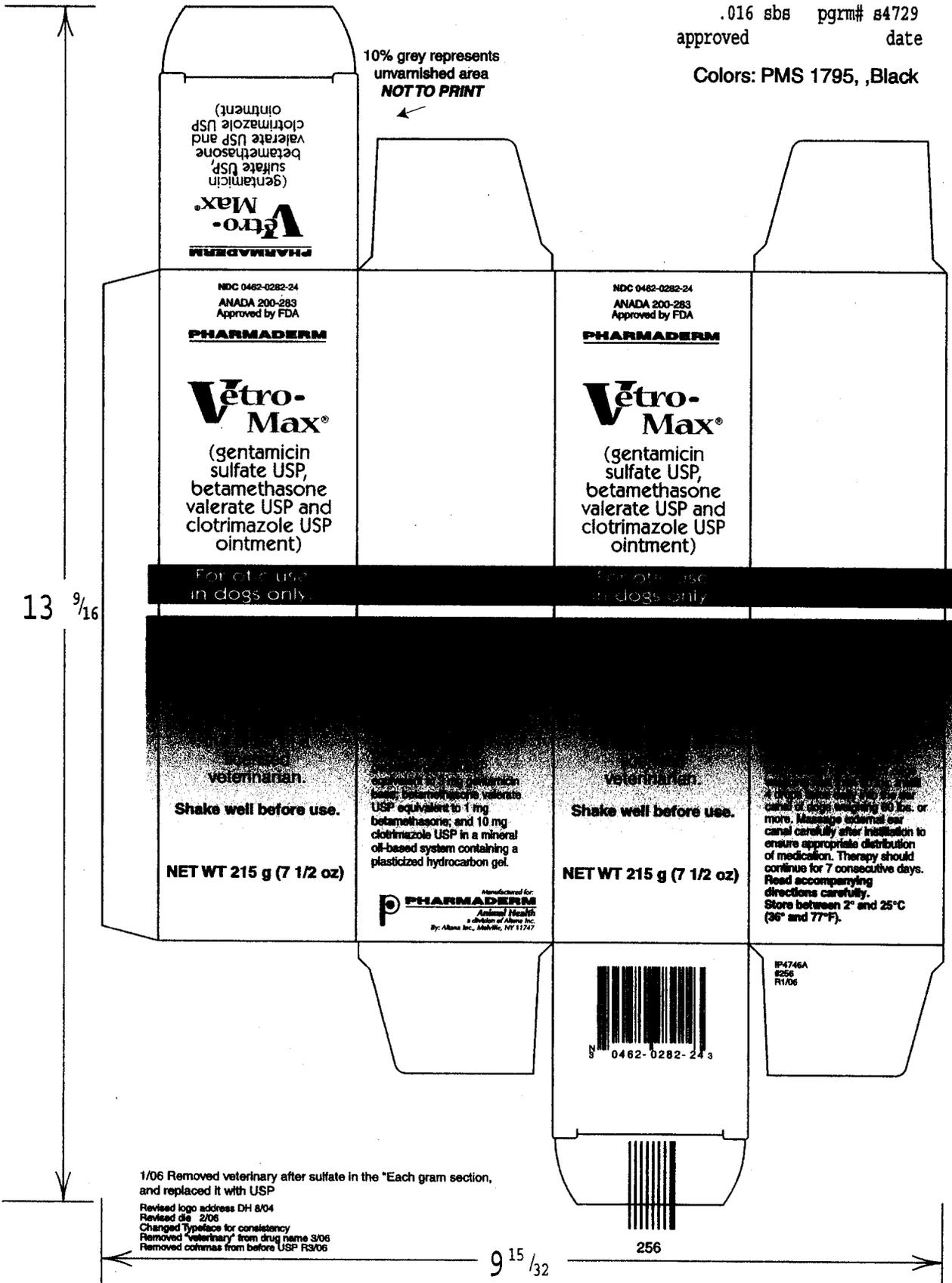
SSC 84' 2+7/32"x 2+7/32 x 7+5/8

reverse tuck, v-notch

.016 sbs pgrm# s4729

approved date

Colors: PMS 1795, ,Black



10% grey represents unvarnished area NOT TO PRINT

(gentamicin sulfate USP, betamethasone valerate USP and clotrimazole USP ointment)
Vetro-Max
PHARMADERM

NDC 0462-0282-24
ANADA 200-283
Approved by FDA
PHARMADERM

Vetro-Max
(gentamicin sulfate USP, betamethasone valerate USP and clotrimazole USP ointment)

NDC 0462-0282-24
ANADA 200-283
Approved by FDA
PHARMADERM

Vetro-Max
(gentamicin sulfate USP, betamethasone valerate USP and clotrimazole USP ointment)

For oral use in dogs only.

For oral use in dogs only.

veterinarian.
Shake well before use.
NET WT 215 g (7 1/2 oz)

Contains 100 mg gentamicin equivalent in the gentamicin base; betamethasone valerate USP equivalent to 1 mg betamethasone; and 10 mg clotrimazole USP in a mineral oil-based system containing a plasticized hydrocarbon gel.

Manufactured for:
PHARMADERM
Animal Health
a division of Alkermes Inc.
By: Alkermes Inc., Marlborough, MA 01752

veterinarian.
Shake well before use.
NET WT 215 g (7 1/2 oz)

Shake well before use. Do not use in dogs weighing 80 lbs. or more. Massage external ear canal carefully after instillation to ensure appropriate distribution of medication. Therapy should continue for 7 consecutive days. Read accompanying directions carefully. Store between 2° and 25°C (36° and 77°F).



IP4746A
#256
R1/06

1/06 Removed veterinary after sulfate in the "Each gram section, and replaced it with USP
Revised logo address DH 8/04
Revised die 2/06
Changed typeface for consistency
Removed "veterinary" from drug name 3/06
Removed commas from before USP R3/06

9 15/32

256

6

SSI-27

7 X 7.5

Added barcode on bottom back 2/06

7.0000

7.5000

Place on frc



ANADA 200-283
Approved by FDA

Vetro-Max®

(gentamicin sulfate USP, betamethasone valerate USP and clotrimazole USP ointment)

VETERINARY

For Otic Use in Dogs Only

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

Keep this and all drugs out of the reach of children.

DESCRIPTION: Each gram of Vetro-Max® ointment contains gentamicin sulfate USP equivalent to 3 mg gentamicin base; betamethasone valerate USP equivalent to 1 mg betamethasone; and 10 mg clotrimazole USP in a mineral oil-based system containing a plasticized hydrocarbon gel.

PHARMACOLOGY:

Gentamicin: Gentamicin sulfate is an aminoglycoside antibiotic active against a wide variety of pathogenic gram-negative and gram-positive bacteria. *In vitro* tests have determined that gentamicin is bactericidal and acts by inhibiting normal protein synthesis in susceptible microorganisms. Specifically, gentamicin is active against the following organisms commonly isolated from canine ears: *Staphylococcus aureus*, other *Staphylococcus* spp., *Pseudomonas aeruginosa*, *Proteus* spp., and *Escherichia coli*.

Betamethasone: Betamethasone valerate is a synthetic adrenocorticoid for dermatologic use. Betamethasone, an analog of prednisolone, has a high degree of corticosteroid activity and a slight degree of mineralocorticosteroid activity. Betamethasone valerate, the 17-valerate ester of betamethasone, has been shown to provide anti-inflammatory and antipruritic activity in the topical management of corticosteroid-responsive otitis externa.

Topical corticosteroids can be absorbed from normal, intact skin. Inflammation can increase percutaneous absorption. Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids.

Clotrimazole: Clotrimazole is a broad-spectrum antifungal agent that is used for the treatment of dermal infections caused by various species of pathogenic dermatophytes and yeasts. The primary action of clotrimazole is against dividing and growing organisms.

In vitro, clotrimazole exhibits fungistatic and fungicidal activity against isolates of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, *Microsporum canis*, *Candida* spp., and *Malassezia pachydermatis* (*Pityrosporum canis*). Resistance to clotrimazole is very rare among the fungi that cause superficial mycoses.

In an induced otitis externa infected with *Malassezia pachydermatis*, 1% clotrimazole in the Vetro-Max® ointment vehicle was effective both microbiologically and clinically in terms of reduction of exudate odor and swelling.

In studies of the mechanism of action, the minimum fungicidal concentration of clotrimazole caused leakage of intra-cellular phosphorus compounds into the ambient medium with concomitant breakdown of cellular nucleic acids and accelerated potassium efflux. These events began rapidly and extensively after addition of the drug.

Clotrimazole is very poorly absorbed following dermal application.

Gentamicin-Betamethasone-Clotrimazole: By virtue of its three active ingredients, Vetro-Max® ointment has antibacterial, anti-inflammatory, and antifungal activity.

In component efficacy studies, the compatibility and additive effect of each of the components were demonstrated. In clinical field trials, gentamicin sulfate, betamethasone valerate, and clotrimazole ointment was effective in the treatment of otitis externa associated with bacteria and *Malassezia pachydermatis*. Gentamicin sulfate, betamethasone valerate, and clotrimazole ointment reduced discomfort, redness, swelling, exudate, and odor, and exerted a strong antimicrobial effect.

INDICATIONS: Vetro-Max® ointment is indicated for the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis*, formerly *Pityrosporum canis*) and/or bacteria susceptible to gentamicin.

CONTRAINDICATIONS: If hypersensitivity to any of the components occurs, treatment should be discontinued and appropriate therapy instituted. Concomitant use of drugs known to induce ototoxicity should be avoided. Do not use in dogs with known perforation of eardrums.

WARNINGS: The use of gentamicin sulfate, betamethasone valerate, and clotrimazole ointment has been associated with deafness or partial hearing loss in a small number of sensitive dogs (eg, geriatric). The hearing deficit is usually temporary. If hearing or vestibular dysfunction is noted during the course of treatment, discontinue use of Vetro-Max® ointment immediately and flush the ear canal thoroughly with a nontoxic solution.

Corticosteroids administered to dogs, rabbits, and rodents during pregnancy have resulted in cleft palate in offspring. Other congenital anomalies including deformed forelegs, phocomelia, and anasarca have been reported in offspring of dogs which received corticosteroids during pregnancy.

Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition if used during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

PRECAUTIONS: Identification of infecting organisms should be made either by microscopic roll smear evaluation or by culture as appropriate. Antibiotic susceptibility of the pathogenic organism(s) should be determined prior to use of this preparation.

If overgrowth of nonsusceptible bacteria, fungi, or yeasts occur, or if hypersensitivity develops, treatment should be discontinued and appropriate therapy instituted.

Place on frc

Place on frc

Place Pharmacode or UPC here, on back side, centered.

CLEARANCES

ALTANA Inc

MATERIAL:

7.0" X 7.5" Product Insert,

SSI Art Base Template For Combo Inserts (Including Any Combo Form, Liquid, Cream, Gel, and Ointment)



Clearance Area



Quiet Zone

All dimension are in inches.

Warning: The smallest carton authorized to be used with this insert is SST-50.

0.0630

SSI-27

7x7.5

All dir are in



Place Pharmaco. or UPC here, on back side. Centered.

here,

Place on fr

Administration of recommended doses of Vetro-Max® ointment beyond 7 days may result in delayed wound healing. Avoid ingestion. Adverse systemic reactions have been observed following the oral ingestion of some topical corticosteroid preparations. Patients should be closely observed for the usual signs of adrenocorticoid overdosage which include sodium retention, potassium loss, fluid retention, weight gain, polydipsia, and/or polyuria. Prolonged use or overdosage may produce adverse immunosuppressive effects.

Use of corticosteroids, depending on dose, duration, and specific steroid, may result in endogenous steroid production inhibition following drug withdrawal. In patients presently receiving or recently withdrawn from corticosteroid treatments, therapy with a rapidly-acting corticosteroid should be considered in especially stressful situations. Before instilling any medication into the ear, examine the external ear canal thoroughly to be certain the tympanic membrane is not ruptured in order to avoid the possibility of transmitting infection to the middle ear as well as damaging the cochlea or vestibular apparatus from prolonged contact.

TOXICOLOGY: Clinical and safety studies with gentamicin sulfate, betamethasone valerate, and clotrimazole ointment have shown a wide safety margin at the recommended dose level in dogs (see PRECAUTIONS/SIDE EFFECTS).

SIDE EFFECTS:

Gentamicin: While aminoglycosides are absorbed poorly from skin, intoxication may occur when aminoglycosides are applied topically for prolonged periods of time to large wounds, burns, or any denuded skin, particularly if there is renal insufficiency. All aminoglycosides have the potential to produce reversible and irreversible vestibular, cochlear, and renal toxicity.

Betamethasone: Side effects such as SAP and SGPT enzyme elevations, weight loss, anorexia, polydipsia, and polyuria have occurred following the use of parenteral or systemic synthetic corticosteroids in dogs. Vomiting and diarrhea (occasionally bloody) have been observed in dogs and cats.

Cushing's syndrome in dogs has been reported in association with prolonged or repeated steroid therapy.

Clotrimazole: The following have been reported occasionally in humans in connection with the use of clotrimazole: erythema, stinging, blistering, peeling, edema, pruritus, urticaria, and general irritation of the skin not present before therapy.

DOSAGE AND ADMINISTRATION: The external ear should be thoroughly cleaned and dried before treatment. Remove foreign material, debris, crusted exudates, etc., with suitable nonirritating solutions. Excessive hair should be clipped from the treatment area. After verifying that the eardrum is intact, instill 4 drops from the 7.5 g and 15 g tube, (2 drops from the 215 g bottle) of Vetro-Max® twice daily into the ear canal of dogs weighing less than 30 lbs. Instill 8 drops from the 7.5 g and 15 g tube, (4 drops from the 215 g bottle) twice daily into the ear canal of dogs weighing 30 lbs. or more. Massage external ear canal carefully after instillation to ensure appropriate distribution of medication. Therapy should continue for 7 consecutive days.

HOW SUPPLIED: Vetro-Max® ointment is available in:

- 7.5 g NDC 0462-0282-75 tubes
- 15 g NDC 0462-0282-15 tubes
- 215 g NDC 0462-0282-24 bottles

Store between 2° and 25°C (36° and 77°F).

Shake well before use when using the 215 g bottle.

TO OPEN: Use cap to puncture seal.



1. Remove entire Applicator Assembly, puncture tube with white portion of the cap.



2. Replace entire Applicator Assembly.



3. To dispense, remove the white portion of the cap.



4. After use replace white cap to close.

IMPORTANT: The opening of this product is covered by a metal tamper-resistant seal. If this seal has been punctured or is not visible, do not use and return product to place of purchase.



PHARMADERM

Animal Health

a division of Altana Inc.

By: Altana Inc., Melville, NY 11747

1128215/F128215
R1/06
#258

7.0000

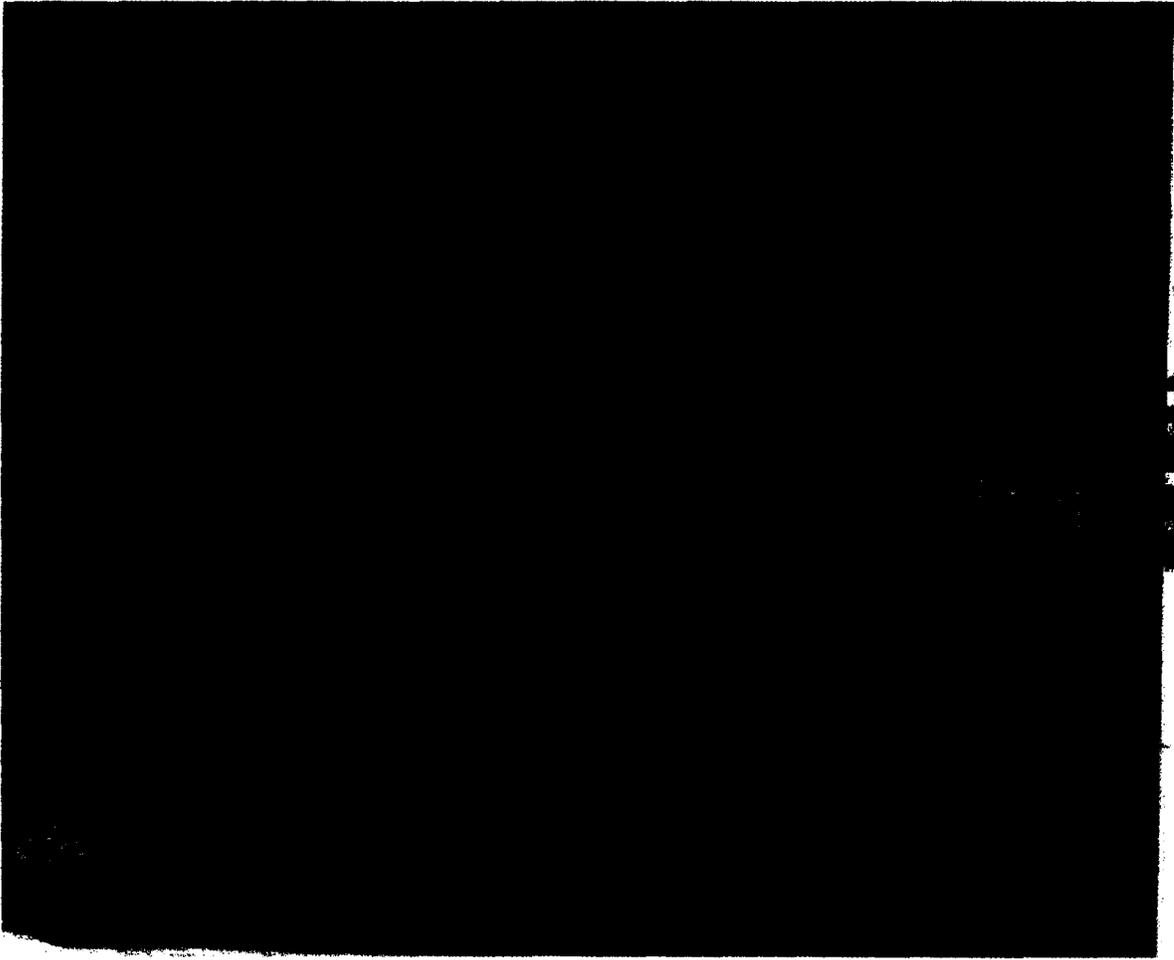
Logo & Product name begins here

Warning: The sma authorized to be u

7.0" X 7.5" Product Insert, SSI Art Base Template For Combo Inserts (Including Any Combo From Liquid Cream, Gel, and Ointment)

ALTANA Inc MATERIAL

TOLERANCES



OTOMAX 15G LABEL
73 mm x 34 mm

2
3
4
5

BMC 001-087-17

Otomax®
 (GENTAMICIN SULFATE, USP,
 BETAMETHASONE VALERATE, USP,
 AND CLOTRIMAZOLE, USP
 OINTMENT)

Keep Out of Reach of Children.

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

NADA 140-898, Approved by FDA.

Schering-Plough Animal Health

LOT EXP

For sale only to licensed veterinarians. Each prescription container of Otomax Ointment contains 15g of ointment. Each 15g container contains 0.1% gentamicin sulfate, 0.1% betamethasone valerate, and 1% clotrimazole. Each 15g container contains 0.1% gentamicin sulfate, 0.1% betamethasone valerate, and 1% clotrimazole. Each 15g container contains 0.1% gentamicin sulfate, 0.1% betamethasone valerate, and 1% clotrimazole. Each 15g container contains 0.1% gentamicin sulfate, 0.1% betamethasone valerate, and 1% clotrimazole.

0061-0387-17 X

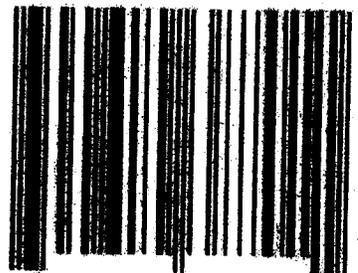
BLACK	
PMS 201	

215 a

[REDACTED]

EXP
LIT

[REDACTED]



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Otomax[®] (GENTAMICIN SULFATE, USP;
BETAMETHASONE VALERATE, USP; AND CLOTRIMAZOLE, USP OINTMENT)

WARNINGS. The use of OTOMAX ointment has been associated with deafness or partial hearing loss in a small number of sensitive dogs (eg, geriatric). The hearing deficit is usually temporary. If hearing or vestibular dysfunction is noted during the course of treatment, discontinue use of OTOMAX ointment immediately and flush the ear canal thoroughly with a nonototoxic solution.

Corticosteroids administered to dogs, rabbits, and rodents during pregnancy have resulted in cleft palate in offspring. Other congenital anomalies including deformed forelegs, phocomelia, and anasarca have been reported in offspring of dogs which received corticosteroids during pregnancy.

Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition if used during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

PRECAUTIONS Identification of infecting organisms should be made either by microscopic roll smear evaluation or by culture as appropriate. Antibiotic susceptibility of the pathogenic organism(s) should be determined prior to use of this preparation.

If overgrowth of nonsusceptible bacteria, fungi, or yeasts occur, or if hypersensitivity develops, treatment should be discontinued and appropriate therapy instituted.

Administration of recommended doses of OTOMAX ointment beyond 7 days may result in delayed wound healing.

Avoid ingestion. Adverse systemic reactions have been observed following the oral ingestion of some topical corticosteroid preparations. Patients should be closely observed for the usual signs of adrenocorticoid overdosage which include sodium retention, potassium loss, fluid retention, weight gain, polydipsia, and/or polyuria. Prolonged use or overdosage may produce adverse immunosuppressive effects.

Use of corticosteroids, depending on dose, duration, and specific steroid, may result in endogenous steroid production inhibition following drug withdrawal. In patients presently receiving or recently withdrawn from corticosteroid treatments, therapy with a rapidly-acting corticosteroid should be considered in especially stressful situations.

Before instilling any medication into the ear, examine the external ear canal thoroughly to be certain the tympanic membrane is not ruptured in order to avoid the possibility of transmitting infection to the middle ear as well as damaging the cochlea or vestibular apparatus from prolonged contact.

TOXICOLOGY Clinical and safety studies with OTOMAX ointment have shown a wide safety margin at the recommended dose level in dogs (see **PRECAUTIONS/SIDE EFFECTS**).

SIDE EFFECTS

Gentamicin: While aminoglycosides are absorbed poorly from skin, intoxication may occur when aminoglycosides are applied topically for prolonged periods of time to large wounds, burns, or any denuded skin, particularly if there is renal insufficiency. All aminoglycosides have the potential to produce reversible and irreversible vestibular, cochlear, and renal toxicity.

Betamethasone: Side effects such as SAP and SGPT enzyme elevations, weight loss, anorexia, polydipsia, and polyuria have occurred following the use of parenteral or systemic synthetic corticosteroids in dogs. Vomiting and diarrhea (occasionally bloody) have been observed in dogs and cats.

Cushing's syndrome in dogs has been reported in association with prolonged or repeated steroid therapy.

Clotrimazole: The following have been reported occasionally in humans in connection with the use of clotrimazole: erythema, stinging, blistering, peeling, edema, pruritus, urticaria, and general irritation of the skin not present before therapy.

DOSAGE AND ADMINISTRATION The external ear should be thoroughly cleaned and dried before treatment. Remove foreign material, debris, crusted exudates, etc., with suitable nonirritating solutions. Excessive hair should be clipped from the treatment area. After verifying that the eardrum is intact, instill 4 drops from the 7.5 g and 15 g tube, and 15 g and 30 g bottle (2 drops from the 215 g bottle) of OTOMAX ointment twice daily into the ear canal of dogs weighing less than 30 lbs. Instill 8 drops from the 7.5 g and 15 g tube, and 15 g and 30 g bottle (4 drops from the 215 g bottle) twice daily into the ear canal of dogs weighing 30 lbs or more. Massage external ear canal carefully after instillation to ensure appropriate distribution of medication. Therapy should continue for 7 consecutive days.

HOW SUPPLIED OTOMAX ointment is available in 7.5 g (NDC 0061-0387-01) and 15 g (NDC 0061-0387-02) tubes as well as in 215 g (NDC 0061-0387-03), 30 g (NDC 0061-0387-08), and 15 g (NDC 0061-0387-17) plastic bottles.

Store between 2° and 25° C (36° and 77° F). Shake well before use when using the 215 g bottle, 30 g bottle, and 15 g bottle.

Made in Canada.

Schering-Plough Animal Health Corp., Union, NJ 07083

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81-475846

B-XXXXXXX



OTOMAX PI
126 mm X 152 mm

F:XXXXXXX

NADA #140-896, Approved by FDA.

PRODUCT INFORMATION

Otomax® (GENTAMICIN SULFATE, USP;
BETAMETHASONE VALERATE, USP; AND CLOTRIMAZOLE, USP OINTMENT)

VETERINARY

For Otic Use in Dogs Only

**CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.
Keep this and all drugs out of the reach of children.**

DESCRIPTION Each gram of OTOMAX ointment contains gentamicin sulfate, USP equivalent to 3 mg gentamicin base; betamethasone valerate, USP equivalent to 1 mg betamethasone; and 10 mg clotrimazole, USP in a mineral oil-based system containing a plasticized hydrocarbon gel.

PHARMACOLOGY

Gentamicin: Gentamicin sulfate is an aminoglycoside antibiotic active against a wide variety of pathogenic gram-negative and gram-positive bacteria. *In vitro* tests have determined that gentamicin is bactericidal and acts by inhibiting normal protein synthesis in susceptible microorganisms. Specifically, gentamicin is active against the following organisms commonly isolated from canine ears: *Staphylococcus aureus*, other *Staphylococcus* spp., *Pseudomonas aeruginosa*, *Proteus* spp., and *Escherichia coli*.

Betamethasone: Betamethasone valerate is a synthetic adrenocorticoid for dermatologic use. Betamethasone, an analog of prednisolone, has a high degree of corticosteroid activity and a slight degree of mineralocorticosteroid activity. Betamethasone valerate, the 17-valerate ester of betamethasone, has been shown to provide anti-inflammatory and antipruritic activity in the topical management of corticosteroid-responsive otitis externa.

Topical corticosteroids can be absorbed from normal, intact skin. Inflammation can increase percutaneous absorption. Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids.

Clotrimazole: Clotrimazole is a broad-spectrum antifungal agent that is used for the treatment of dermal infections caused by various species of pathogenic dermatophytes and yeasts. The primary action of clotrimazole is against dividing and growing organisms.

In vitro, clotrimazole exhibits fungistatic and fungicidal activity against isolates of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, *Microsporum canis*, *Candida* spp., and *Malassezia pachydermatis* (*Pityrosporum canis*). Resistance to clotrimazole is very rare among the fungi that cause superficial mycoses.

In an induced otitis externa infected with *Malassezia pachydermatis*, 1% clotrimazole in the OTOMAX vehicle was effective both microbiologically and clinically in terms of reduction of exudate, odor, and swelling.

In studies of the mechanism of action, the minimum fungicidal concentration of clotrimazole caused leakage of intracellular phosphorus compounds into the ambient medium with concomitant breakdown of cellular nucleic acids and accelerated potassium efflux. These events began rapidly and extensively after addition of the drug.

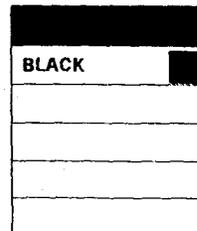
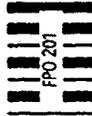
Clotrimazole is very poorly absorbed following dermal application.

Gentamicin-Betamethasone-Clotrimazole: By virtue of its three active ingredients, OTOMAX ointment has antibacterial, anti-inflammatory, and antifungal activity.

In component efficacy studies, the compatibility and additive effect of each of the components were demonstrated. In clinical field trials, OTOMAX ointment was effective in the treatment of otitis externa associated with bacteria and *Malassezia pachydermatis*. OTOMAX ointment reduced discomfort, redness, swelling, exudate, and odor, and exerted a strong antimicrobial effect.

INDICATIONS OTOMAX ointment is indicated for the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis*, formerly *Pityrosporum canis*) and/or bacteria susceptible to gentamicin.

CONTRAINDICATIONS If hypersensitivity to any of the components occurs, treatment should be discontinued and appropriate therapy instituted. Concomitant use of drugs known to induce ototoxicity should be avoided. Do not use in dogs with known perforation of eardrums.





PHARMA CODE
FOR POSITION ONLY
FPO 141

CODE AREA
12 MM

(GENTAMICIN SULFATE, USP,
BETAMETHASONE VALERATE, USP, AND
CLOTRIMAZOLE, USP OINTMENT)

Otomax[®]

For otic use in dogs only.

Indications: OTOMAX[®] (gentamicin sulfate, USP; betamethasone valerate, USP; and clotrimazole, USP ointment) is indicated for the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis*, formerly *Pityrosporum canis*) and/or bacteria susceptible to gentamicin.

Each gram contains: gentamicin sulfate, USP equivalent to 3 mg gentamicin base; betamethasone valerate, USP equivalent to 1 mg betamethasone; and 10 mg clotrimazole, USP in a mineral oil-based system containing a plasticized hydrocarbon gel.

Dosage and Administration: The external ear should be properly cleaned and dried before treatment. Remove foreign material, debris, crusted exudates, etc., with suitable nonirritating solutions. Excessive hair should be clipped from the treatment area. After verifying that the eardrum is intact, instill 4 drops of OTOMAX ointment twice daily into the ear canal of dogs weighing less than 30 lbs. Instill 8 drops twice daily into the ear canal of dogs weighing 30 lbs or more. Massage external ear canal carefully after instillation to ensure appropriate distribution of medication. Therapy should continue for 7 consecutive days.

Read accompanying directions carefully.

Store between 2° and 25° C (36° and 77° F).

Shake well before use.

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For otic use in dogs only.

Made in Canada.

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Schering-Plough
Animal Health

NDC 0061-0387-17

Otomax[®]

(GENTAMICIN SULFATE, USP;
BETAMETHASONE VALERATE, USP;
AND CLOTRIMAZOLE, USP OINTMENT)

Keep Out of Reach of Children.

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

NADA #140-896,
Approved by FDA.

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FPO 141
PHARMA CODE
FOR POSITION ONLY

PMS 201

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