GENTIZOL - gentamicin sulfate, betamethasone valerate, and clotrimazole ointment
MWI

GENTAMICIN SULFATE USP, BETAMETHASONE VALERATE, USP, and CLOTRIMAZOLE, USP OINTMENT

ANADA #200-229, Approved by FDA
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 gentamicin-betamethasone-clotrimazole 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 anti-pruritic 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 gentamicin-betamethasone-clotrimazole 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 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, gentamicin-betamethasone-clotrimazole 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-betamethasone-clotrimazole was effective in the treatment of otitis externa associated with bacteria and *Malassezia pachydermatis*. Gentamicin sulfate USP, Betamethasone valerate, USP and Clotrimazole, USP ointment reduced discomfort, redness, swelling, exudate, and odor, and exerted a strong antimicrobial effect.

INDICATIONS: Gentamicin-betamethasone-clotrimazole 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-betamethasone-clotrimazole ointment has been associated with deafness or partial hearing loss in a small number of sensitive dogs (e.g. geriatric). The hearing deficit is usually temporary. If hearing or vestibular dysfunction is noted during the course of treatment, discontinue use of gentamicin-betamethasone-clotrimazole ointment immediately and flush the ear canal thoroughly with a non-ototoxic 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 gentamicin-betamethasone-clotrimazole 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 USP, Betamethasone valerate, USP and Clotrimazole USP 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 non-irritating solutions. Excessive hair should be clipped from the treatment area. After verifying that the eardrum is intact, instill 4 drops (2 drops from the 215 g. bottle) of gentamicin-betamethasone-clotrimazole ointment twice daily into the ear canal of dogs weighing less than 30 lbs. Instill 8 drops (4 drops from the 215 g. bottle) twice daily into the ear canal of dogs weighing 30 lbs. or more. Therapy should continue for 7 consecutive days.

HOW SUPPLIED: Gentamicin-betamethasone-clotrimazole ointment is available in 7.5 gram and 15 gram tubes
as well as in 10 gram, 15 gram, 25 gram and 215 gram plastic bottles.

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

January 2001

MED-PHARMEX, INC.
POMONA, CA 91767

VET one®

Gentizol™

(Gentamicin Sulfate, USP Betamethasone Valerate, USP and Clotrimazole, USP Ointment)

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

KEEP OUT OF REACH OF CHILDREN

For otic use in dogs only.

NET CONTENTS: 7.5 g

Expiration date and lot number on crimp.

Indications: Gentizol™ 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.

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

NDC 13985-006-75
ANADA 200-229
Approved by FDA

V1 501006

Distributed by: MWI
Boise, ID 83705
(888) 694-8381
www.VetOne.net
Rev. 10/13

VETone®

Gentizol™

(Gentamicin Sulfate, USP Betamethasone Valerate, USP and Clotrimazole, USP Ointment)

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

KEEP OUT OF REACH OF CHILDREN
NET CONTENTS: 15 g

For otic use in dogs only.
Expiration date and lot number on crimp.

Gentizol™ Ointment

(Gentamicin Sulfate, USP Betamethasone Valerate, USP and Clotrimazole, USP Ointment)

Indications: Gentizol™ 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.

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

NDC 13985 006 15
ANADA 200-229
Approved by FDA

V1 502006

Distributed by: MWI
Boise, ID 83705
(888) 694-8381
www.VetOne.net
Rev. 10/13

NDC 13985-006-10

10 g

VETone®

Gentizol™

(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.

For otic use in dogs only.

ANADA 200-229
Approved by FDA

V1 505006

INDICATIONS: Gentizol™ 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.

Net Contents: 10 g

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

Distributed by: MWI
Boise, ID 83705
(888) 694-8381
www.VetOne.net
Rev. 10/13

Lot #/Exp. Date

NDC 13985-006-45

15 g

VETone®

Gentizol™

(Gentamicin Sulfate, USP Betamethasone Valerate, USP and Clotrimazole, USP)

Ointment

For Otic Use in Dogs Only

Keep out of reach of children.

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

ANADA #200-229, Approved by FDA

V1 506006

Net Contents: 15 g

INDICATIONS: Gentizol™ 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.

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

Distributed by: MWI
Boise, ID 83705
(888) 694-8381
www.VetOne.net

Rev. 10/13

MADE IN USA

TAKE TIME
OBSERVE LABEL DIRECTIONS

Lot #/ Exp. Date:

NDC 13985-006-25

25 g

VETone®

Gentizol™

(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.

For otic use in dogs only.

ANADA 200-229
Approved by FDA

V1 503006

INDICATIONS: Gentizol™ 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.

Net Contents: 25 g

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

Distributed by: MWI
Boise, ID 83705
(888) 694-8381
www.VetOne.net
Rev. 10/13

Lot #/Exp. Date

INDICATIONS: Gentizol™ 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 Gentizol™ 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 30lbs. 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°C and 25°C (36°F and 77°F).

Shake well before use.

Distributed by: MWI
Boise, ID 83705
(888) 694-8381
www.VetOne.net

TAKE TIME
OBSERVE LABEL DIRECTIONS

Rev. 10/13
MADE IN USA

Lot #/Exp. Date

GENTIZOL

gentamicin sulfate, betamethasone valerate, and clotrimazole ointment

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:13985-006
Route of Administration	AURICULAR (OTIC)		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
GENTAMICIN SULFATE (UNII: 8X7386QRLV) (GENTAMICIN - UNII:T6Z9V48IKG)	GENTAMICIN	3 mg in 1 g
BETAMETHASONE VALERATE (UNII: 9IFA5XM7R2) (BETAMETHASONE - UNII:9842X06Q6M)	BETAMETHASONE	1 mg in 1 g
CLOTRIMAZOLE (UNII: G07GZ97H65) (CLOTRIMAZOLE - UNII:G07GZ97H65)	CLOTRIMAZOLE	10 mg in 1 g

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date

1	NDC:13985-006-75	7.5 g in 1 TUBE		
2	NDC:13985-006-15	15 g in 1 TUBE		
3	NDC:13985-006-10	10 g in 1 BOTTLE, PLASTIC		
4	NDC:13985-006-45	15 g in 1 BOTTLE, PLASTIC		
5	NDC:13985-006-25	25 g in 1 BOTTLE, PLASTIC		
6	NDC:13985-006-40	215 g in 1 BOTTLE, PLASTIC		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200229	01/01/2001	

Labeler - MWI (019926120)

Registrant - Med-Pharmex, Inc (025353699)

Establishment

Name	Address	ID/FEI	Business Operations
Med-Pharmex, Inc		025353699	manufacture

Revised: 1/2001 MWI