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MWI® Animal Health
AmerisourceBergen

NO ADRENOCORTICAL SUPPRESSION WITH MOMETAMAX® IN DOGS WITH OTITIS EXTERNA[2]

- All dogs treated with Mometamax® had normal corticotropin stimulation test results
- One or more dogs treated with other therapies developed adrenocortical suppression

Corticotropin stimulation test results† of dogs after 7 days of topical otic therapy for otitis externa

Medication	No. of dogs	No. (%) below range	No. (%) in range	No. (%) above range
Mometamax®	9	0 (0)	9 (100)	0 (0)
Tresaderm®	8	4 (50)††	4 (50)	0 (0)
Panolog®	12	2 (17)	8 (67)	2 (17)
DVMax™	11	1 (9)	9 (82)	1 (9)

Adapted from Reeder CJ, et al. *Vet Ther.* 2008;9(2):111-121.
† Based on serum from whole blood samples collected 2 hours after corticotropin gel (2.2 U/kg) was administered in epaxial muscle. Cortisol analyses were performed by an independent commercial laboratory using a standardized radioimmunoassay kit previously evaluated for use in dogs. Normal range: 8-17 mg/dL.
†† $P = 0.03$ versus dogs treated with Mometamax®
• Randomized, double-blinded study
• Topical otic therapy for 1 week with Mometamax® and other treatments

Mometamax® Otic Suspension should be discontinued if any hypersensitivity to its components occurs. Do not use in dogs with known tympanic perforation. For side effects and warnings, please see accompanying Product Information.

FOR DECADES, VETERINARIANS HAVE RELIED ON MERCK ANIMAL HEALTH FOR ADVANCED RESEARCH AND DEVELOPMENT OF NOVEL OTIC THERAPIES.

Mometamax® is the most prescribed product for treatment of otitis externa.[3]

Mometamax® delivers once-a-day treatment and a soothing formulation to promote compliance and treatment success.[3]

"Owner was very happy with response to treatment with Mometamax, and the dog was acting so much better."
Dr. Anderson, Veterinarian, Idaho

"Mometamax is the best thing ever. Easy to give, so clean, and I love the once-a-day treatment; but best of all, it started to work so fast."
Loretta Howard, Dog Owner, Maryland

THE ONLY PRODUCTS YOU NEED TO TREAT OTITIS EXTERNA

MOMETAMAX® AND POSATEX® PROVIDE CLEAR ONCE-A-DAY CHOICES FOR YOUR OTITIS EXTERNA NEEDS

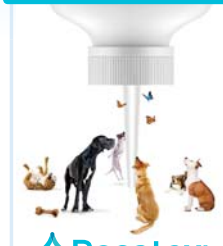
FOR MILD TO MODERATE CASES

Once-a-day Mometamax®
(Gentamicin Sulfate, USP, Mometasone Furoate Monohydrate and Clotrimazole, USP, Otic Suspension)

YOUR ONCE-A-DAY CHOICE FOR MILD TO MODERATE CASES

Mometamax® rapidly reduces inflammation and swelling for increased patient comfort.

FOR SEVERE AND CHRONIC CASES



Posatex® Otic Suspension
(Orbifloxacin, Mometasone Furoate Monohydrate and Posaconazole, Suspension)

Now once-a-day POSATEX® Otic Suspension adds increased potency to your treatment options, with novel active ingredients:

- **Mometasone Furoate Monohydrate**
  Proven safe and effective for rapid relief of inflammation
- **Orbifloxacin**
  Proven efficacy against bacteria associated with canine otitis externa including *Pseudomonas aeruginosa*
- **Posaconazole**
  Novel antifungal agent perfect for cases with severe *Malassezia*

POSATEX® Otic Suspension is contraindicated in dogs with known or suspected hypersensitivity to quinolones, mometasone furoate monohydrate, or posaconazole. Do not use in dogs with known tympanic perforation. The safe use in dogs used for breeding purposes, during pregnancy or in lactating bitches, has not been evaluated.

For technical support, call MERCK Animal Health Technical Service www.merck-animal-health-usa.com
TECHNICAL SERVICE (MON.-FRI., 8:30 AM - 5 PM, EST): 1-800-224-5318
CUSTOMER SERVICE (MON.-FRI., 8 AM - 7 PM, EST): 1-800-521-5767

1. Rubin J, Walker RD, Bilkovsky R, et al. Antimicrobial resistance and genetic characterization of fluoroquinolone resistance of *Pseudomonas aeruginosa* isolated from canine infections. *Vet Microbiol.* 2008;131:164-172.
2. Reeder CJ, Griffin CE, Polissar NL, et al. Comparative adrenocortical suppression in dogs with otitis externa following topical otic administration of four different glucocorticoid-containing medications. *Vet Ther.* 2008;9(2):111-121.
3. Data on File.

MERCK Animal Health

MOMETAMAX® IS THE PROVEN STANDARD IN FIRST-LINE OTITIS EXTERNA TREATMENT.

Once-a-day Mometamax®
(Gentamicin Sulfate, USP, Mometasone Furoate Monohydrate and Clotrimazole, USP, Otic Suspension)

MOMETAMAX® OFFERS A PROVEN TREATMENT COMBINATION

1- Mometasone Furoate Monohydrate: Anti-inflammatory Action

- Rapidly controls inflammation to reduce related pain and irritation

2- Clotrimazole: Antifungal Control

- Documented efficacy against *Malassezia pachydermatis*

3- Gentamicin: Antibacterial Effect

- Trusted antibiotic with low incidence of reported bacterial resistance[1]

PATHOGENESIS AND TREATMENT OF OTITIS EXTERNA

Once-a-day
Mometamax®
(Gentamicin Sulfate, USP, Mometasone Furoate Monohydrate and Clotrimazole, USP, Otic Suspension

F-27078915
NADA #141-177. Approved by FDA.

MOMETAMAX®
(GENTAMICIN SULFATE, USP; MOMETASONE FUROATE MONOHYDRATE; AND CLOTRIMAZOLE, USP, OTIC SUSPENSION)

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 MOMETAMAX Otic Suspension contains gentamicin sulfate, USP equivalent to 3 mg gentamicin base; mometasone furoate monohydrate equivalent to 1 mg mometasone; 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 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. In clinical trials, gentamicin was shown to have a range of activity against the following organisms commonly isolated from infected canine ears: *Pseudomonas* spp. (including *P. aeruginosa*), coagulase-positive staphylococci, *Enterococcus faecalis, Proteus mirabilis* and beta-hemolytic streptococci.

Mometasone: Mometasone furoate monohydrate is a synthetic adrenocorticoid characterized by a novel (2') furoate 17-ester having chlorine at the 9 and 21 positions, which have shown to possess high topical potency.

Systemic absorption of mometasone furoate ointment was found to be minimal (2%) over 1 week when applied topically to dogs with intact skin. In a 6-month dermal toxicity study using 0.1% mometasone ointment on healthy intact skin in dogs, systemic effects typical of corticosteroid that therapy were noted.

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the integrity of the epidermal barrier. 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 dermatophytes and yeast. 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*. Resistance to clotrimazole is very rare among the fungi that cause superficial mycoses. In an induced otitis externa study using dogs infected with *Malassezia pachydermatis*, 1% clotrimazole in the vehicle formulation 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-Mometasone-Clotrimazole: By virtue of its three active ingredients, MOMETAMAX Otic Suspension has antibacterial, anti-inflammatory, and antifungal activity. In clinical field trials, MOMETAMAX Otic Suspension was effective in the treatment of otitis externa associated with bacteria and *Malassezia pachydermatis*. MOMETAMAX Otic Suspension reduced discomfort, redness, swelling, exudate, and odor.

INDICATIONS MOMETAMAX Otic Suspension is indicated for the treatment of otitis externa in dogs caused by susceptible strains of yeast (*Malassezia pachydermatis*) and bacteria (*Pseudomonas* spp. [including *P. aeruginosa*], coagulase-positive staphylococci, *Enterococcus faecalis, Proteus mirabilis,* and beta-hemolytic streptococci).

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 these components 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 MOMETAMAX Otic Suspension 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 that received corticosteroids during pregnancy.

Field 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 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.

Administration of recommended doses of MOMETAMAX Otic Suspension beyond 7 days may result in delayed wound healing.

If overgrowth of nonsusceptible bacteria or fungi occurs, treatment should be discontinued and appropriate therapy instituted.

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 adrenocortioid 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.

TOXICOLOGY Field and safety studies with MOMETAMAX Otic Suspension have shown a wide safety margin at the recommended dose level in dogs (see **PRECAUTIONS/ADVERSE REACTIONS**).

ADVERSE REACTIONS

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.

Mometasone: ALP (SAP) and ALT (SGPT) enzyme elevations, weight loss, anorexia, polydipsia, polyuria, neutrophilia, and lymphopenia have occurred following the use of parenteral, high-dose, and/or prolonged or systemic synthetic corticosteroids in dogs. 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.

MOMETAMAX Otic Suspension: In field studies following once-daily treatment with MOMETAMAX Otic Suspension, ataxia, proprioceptive deficits, and increased water consumption were observed in less than 1% of 164 dogs. In a field study following twice-daily treatment with MOMETAMAX Otic Suspension, inflammation of the pinna and diarrhea were observed in less than 1% of 141 dogs.

DOSAGE AND ADMINISTRATION

The external ear canal should be thoroughly cleaned and dried before treatment. Verify that the eardrum is intact. For dogs weighing less than 30 lbs, instill 4 drops from the 7.5 g, 15 g, and 30 g bottles (2 drops from the 215 g bottle) of MOMETAMAX Otic Suspension once daily into the ear canal. For dogs weighing 30 lbs or more, instill 8 drops from the 7.5 g, 15 g, and 30 g bottles (4 drops from the 215 g bottle) once daily into the ear canal. Therapy should continue for 7 consecutive days.

HOW SUPPLIED MOMETAMAX Otic Suspension is available in 7.5 g (NDC 0061-1246-05), 15 g (NDC 0061-1246-04), 30 g (NDC 0061-1246-01), and 215 g (NDC 0061-1246-02) plastic bottles.

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

For patent information:
http://www.merck.com/product/patent/home.html

Intervet Inc. (d/b/a Merck Animal Health)
Madison, NJ 07940

Made in Canada.

Rev. 04/15 B-27078915
81-497143

PRODUCT INFORMATION

187771 R1

Posatex® Otic Suspension
(Orbifloxacin, Mometasone Furoate Monohydrate and Posaconazole, Suspension)

Antibacterial, anti-inflammatory, antifungal

For Otic Use in Dogs Only

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

Federal law prohibits the extralabel use of this drug in food-producing animals.

DESCRIPTION: Each gram of POSATEX® Otic Suspension contains 10 mg of orbifloxacin; mometasone furoate monohydrate equivalent to 1 mg mometasone furoate; and 1 mg of posaconazole in a mineral oil based system containing a plasticized hydrocarbon gel.
Four drops of POSATEX® Otic Suspension delivers approximately 1.0 mg orbifloxacin, 0.1 mg of mometasone furoate monohydrate, and 0.1 mg of posaconazole.

INDICATIONS: POSATEX® Otic Suspension is indicated for the treatment of otitis externa in dogs associated with susceptible strains of yeast (*Malassezia pachydermatis)* and bacteria (coagulase positive staphylococci, *Pseudomonas aeruginosa,* and *Enterococcus faecalis).*

DOSAGE AND ADMINISTRATION: Shake well before use. For dogs weighing less than 30 lbs. instill 4 drops of POSATEX® Otic Suspension once daily into the ear canal. For dogs weighing 30 lbs. or more, instill 8 drops once daily into the ear canal. Therapy should continue for 7 consecutive days.

CONTRAINDICATIONS: POSATEX® Otic Suspension is contraindicated in dogs with known or suspected hypersensitivity to quinolones, mometasone furoate monohydrate, or posaconazole. Do not use in dogs with known tympanic perforation (see **PRECAUTIONS**).

WARNINGS:
Human Warnings: Not for use in humans. Keep out of reach of children.
Animal Warnings: Do not administer orally. Immediately discontinue use of POSATEX® Otic Suspension if hearing loss is observed during treatment (see **ADVERSE REACTIONS**).

PRECAUTIONS: The use of POSATEX® Otic Suspension in dogs with perforated tympanic membranes has not been evaluated. The integrity of the tympanic membrane should be confirmed before administering this product.
Avoid prolonged or repeated use of POSATEX® Otic Suspension. Long-term use of topical otic corticosteroids has been associated with adrenocortical suppression and iatrogenic hyperadrenocorticism in dogs (see **ANIMAL SAFETY**).
The safe use of POSATEX® Otic Suspension in dogs used for breeding purposes, during pregnancy or in lactating bitches, has not been evaluated. The systemic administration of quinolones has been shown to produce cartilage erosions of weight bearing joints and other signs of arthropathy in immature animals of various species.

ADVERSE REACTIONS: In the field study, 143 dogs were treated with POSATEX® Otic Suspension. Of those, 1 dog with bilateral otitis externa developed hearing loss. POSATEX® Otic Suspension treatment was discontinued and the condition resolved after one week.

To report suspected adverse reactions, call 1-800-224-5318.

For a copy of the Material Safety Data Sheet (MSDS) call 1-800-770-8878.

CLINICAL PHARMACOLOGY:
Orbifloxacin: Orbifloxacin is a synthetic fluoroquinolone antibacterial agent. The bactericidal action of fluoroquinolones is concentration-dependent and results from interference with bacterial DNA gyrase and topoisomerase IV. Since these enzymes are needed for bacterial DNA synthesis and transcription, fluoroquinolones disrupt bacterial replication and lead to bacterial cell death.
Mometasone: Mometasone furoate monohydrate is a topical corticosteroid characterized by a (2') furoate 17-ester having chlorine at the 9 and 21 positions.
Posaconazole: Posaconazole is a broad-spectrum triazole antifungal agent. The mechanism by which triazoles exert fungicidal action involves the selective inhibition of the enzyme lanosterol a C1 4 demethylase (a microsomal cytochrome P-450- dependent enzyme) involved in ergosterol biosynthesis in yeasts and filamentous fungi.
Systemic absorption of the active ingredients was determined in single-dose radiolabelled studies with ^{14}C-orbifloxacin, ^{3}H-mometasone furoate, and ^{14}C-posaconazole contained within the POSATEX® Otic Suspension formulation and placed into the ear canals of normal beagle dogs. Most of the absorption occurred in the first few days after administration. The extent of percutaneous absorption of topical medications is influenced by many factors including the integrity of the epidermal barrier. Inflammation can increase the percutaneous absorption of drugs.

EFFECTIVENESS: The effectiveness of POSATEX® Otic Suspension was evaluated in a placebo-controlled, double-blind, multi-site field study. One hundred and ninety one dogs with naturally occurring clinical otitis externa associated with both yeast and bacteria were randomly allocated to either POSATEX® Otic Suspension or placebo ointment. Of the 160 dogs evaluated for effectiveness, 122 were treated with POSATEX® Otic Suspension and 38 were treated with placebo ointment. Treatments were administered once daily for 7 consecutive days. Assessment of effectiveness was based on improvement in clinical signs at re-evaluation 2-7 days following administration of the last dose.

Compared to the placebo, a significant percent of dogs treated with POSATEX® Otic Suspension showed improvement in clinical signs (discomfort, erythema, and swelling) caused by otitis externa associated with one or more of the following organisms: *Malassezia pachydermatis*, coagulase positive staphylococci, *Pseudomonas aeruginosa*, and *Enterococcus faecalis.*

Percent of Dogs Showing Improvement in Clinical Signs of Otitis Externa

Clinical Sign	POSATEX® Otic Suspension Group	Placebo Group	Significance
Discomfort	88%	45%	p<0.0001
External Ear Canal Erythema	81%	39%	p<0.0001
External Ear Canal Swelling	83%	49%	p=0.0001

ANIMAL SAFETY: POSATEX® Otic Suspension was administered at 1,3, and 5 times the recommended dosage for 21 consecutive days. The control group received the vehicle in both ears at the clinical dose given five times per day. There was a slight decrease in serum cortisol concentration after ACTH stimulation on Day 21 in the 5X group. Erythema was noted in all groups. Aural pain, swelling, or heat were each noted in 3 separate dogs in the 5X group.

STORAGE INFORMATION: Store at temperatures between 2°-30°C (35.6°-86°F).

Shake well before use.

HOW SUPPLIED: POSATEX® Otic Suspension is available in 7.5 g, 15 g, and 30 g plastic bottles.
NADA# 141-266, Approved by FDA.

Made in Germany

MERCK Animal Health