

Neoplasms metastatic to the thyroid gland

Lester D.R. Thompson, MD, FASCP

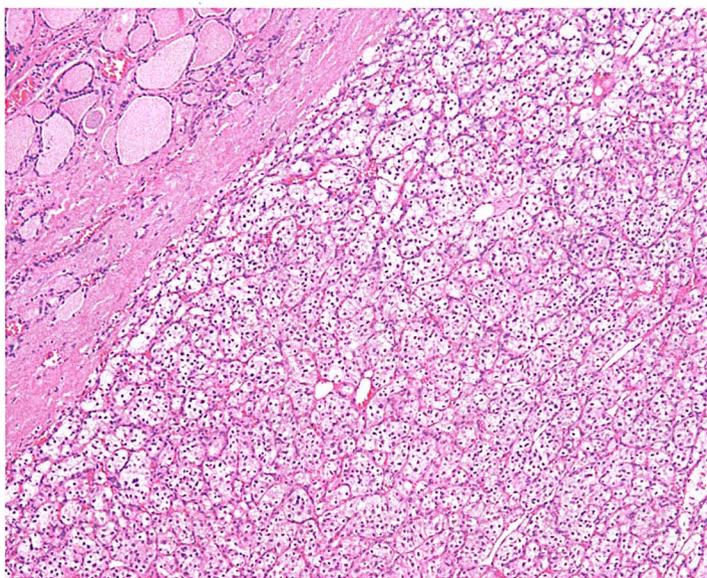


Figure 1. Low-power view shows an encapsulated nodule of metastatic renal cell carcinoma in the thyroid gland. Note the uninvolved thyroid follicles in the upper left.

Tumors that occur in the thyroid gland as a result of lymph or vascular spread from distant sites are considered to represent metastatic disease rather than a direct extension of a primary from an adjacent organ. Metastatic deposits are identified at a higher frequency in abnormal glands—that is, those with adenomatoid nodules, thyroiditis, and follicular neoplasms. Further, metastatic deposits may be found within primary thyroid tumors, such as a renal cell carcinoma metastatic to a thyroid papillary carcinoma. Although a thyroid gland mass may be the presenting clinical sign, it is more often the underlying thyroid gland disease (e.g., thyroiditis, adenomatoid nodules) that prompts clinical evaluation. The thyroid gland metastatic deposit is the initial presentation of an occult

primary tumor in as many as 40% of patients. Carcinomas are the most common metastatic tumors from (in order of frequency) the kidney (figure 1), lung, breast (figure 2), and stomach; melanoma is less common.

Multifocal and bilateral disease is common, although some single masses are seen. The highly vascularized thyroid gland is quite susceptible to metastatic deposits. The metastatic deposits morphologically and architecturally resemble the primary site, yielding a distinctly different histologic appearance from thyroid gland primaries. However, clear-cell carcinomas (e.g., renal cell carcinoma) and small-cell carcinomas (e.g., neuroendocrine carcinoma) may resemble a primary thyroid gland tumor. In such a setting, immunohistochemistry analysis will help with the

HOW CAN YOU MISS?



For More Otitis Externa Cures than CORTISPORIN* Otic, the Medal Goes to the #1 Otic Drop Among Otolaryngologists and Pediatricians.^{1,2}

The fast lane to more cures lies in reducing pain and inflammation sooner.³ CIPRODEX® Otic, with the highly efficient anti-inflammatory dexamethasone, delivers greater OE pain relief by day 2 than CORTISPORIN Otic, and achieves a significantly higher rate of treatment success.^{3,4} Get them back in the swim—fast—with CIPRODEX® Otic.

CIPRODEX® Otic is indicated in patients 6 months and older for acute otitis externa due to *Staphylococcus aureus* and *Pseudomonas aeruginosa*. CIPRODEX® Otic is contraindicated in patients with a history of hypersensitivity to ciprofloxacin, other quinolones and viral infections. If the infection is not improved after one week of treatment, cultures should be obtained to guide further treatment. Most commonly reported adverse reactions in clinical trials in AOE patients: pruritus (1.5%), ear debris (0.6%), superimposed ear infection (0.6%), ear congestion (0.4%), ear pain (0.4%) and erythema (0.4%).

CIPRODEX is a registered trademark of Bayer AG. Licensed to Alcon, Inc. by Bayer AG.

*Trademark is the property of its owner.

Please see adjacent page for brief summary of prescribing information.

Alcon®

ALCON LABORATORIES, INC.

Fort Worth, Texas 76134

www.ciprodex.com

©2006 Alcon, Inc.

4/06

CDX06503JA

CIPRODEX®
(ciprofloxacin 0.3% and dexamethasone 0.1%)
STERILE OTIC SUSPENSION

All together better.

CIPRODEX[®]

(ciprofloxacin 0.3% and dexamethasone 0.1%)
STERILE OTIC SUSPENSION

DESCRIPTION

CIPRODEX[®] (ciprofloxacin 0.3% and dexamethasone 0.1%) Sterile Otic Suspension contains the synthetic broad-spectrum antibacterial agent, ciprofloxacin hydrochloride, combined with the anti-inflammatory corticosteroid, dexamethasone, in a sterile, preserved suspension for otic use. Each mL of CIPRODEX[®] Otic contains ciprofloxacin hydrochloride (equivalent to 3 mg ciprofloxacin base), 1 mg dexamethasone, and 0.1 mg benzalkonium chloride as a preservative. The inactive ingredients are boric acid, sodium chloride, hydroxyethyl cellulose, tyloxapol, acetic acid, sodium acetate, edetate disodium, and purified water. Sodium hydroxide or hydrochloric acid may be added for adjustment of pH.

Ciprofloxacin, a fluoroquinolone is available as the monohydrochloride monohydrate salt of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid. The empirical formula is C₁₇H₁₈FN₃O₃·HCl·H₂O. Dexamethasone, 9-fluoro-11(β),17,21-trihydroxy-16(α)-methylpregna-1,4-diene-3,20-dione, is an anti-inflammatory corticosteroid. The empirical formula is C₂₂H₂₉F₂O₅.

CLINICAL PHARMACOLOGY

Pharmacokinetics: Following a single bilateral 4-drop (total dose = 0.28 mL, 0.84 mg ciprofloxacin, 0.28 mg dexamethasone) topical otic dose of CIPRODEX[®] Otic to pediatric patients after tympanostomy tube insertion, measurable plasma concentrations of ciprofloxacin and dexamethasone were observed at 6 hours following administration in 2 of 9 patients and 5 of 9 patients, respectively.

Mean ± SD peak plasma concentrations of ciprofloxacin were 1.39 ± 0.880 ng/mL (n=9). Peak plasma concentrations ranged from 0.543 ng/mL to 3.45 ng/mL and were on average approximately 0.1% of peak plasma concentrations achieved with an oral dose of 250-mg[®]. Peak plasma concentrations of ciprofloxacin were observed within 15 minutes to 2 hours post dose application. Mean ± SD peak plasma concentrations of dexamethasone were 1.14 ± 1.54 ng/mL (n=9). Peak plasma concentrations ranged from 0.135 ng/mL to 5.10 ng/mL and were on average approximately 14% of peak concentrations reported in the literature following an oral 0.5-mg tablet dose[®]. Peak plasma concentrations of dexamethasone were observed within 15 minutes to 2 hours post dose application. Dexamethasone has been added to aid in the resolution of the inflammatory response accompanying bacterial infection (such as otitis in pediatric patients with AOM with tympanostomy tubes).

Microbiology: Ciprofloxacin has *in vitro* activity against a wide range of gram-positive and gram-negative microorganisms. The bactericidal action of ciprofloxacin results from interference with the enzyme, DNA gyrase, which is needed for the synthesis of bacterial DNA. Cross-resistance has been observed between ciprofloxacin and other fluoroquinolones. There is generally no cross-resistance between ciprofloxacin and other classes of antibacterial agents such as beta-lactams or aminoglycosides.

Ciprofloxacin has been shown to be active against most isolates of the following microorganisms, both *in vitro* and clinically in otic infections as described in the **INDICATIONS AND USAGE** section.

Aerobic and facultative gram-positive microorganisms: *Staphylococcus aureus*, *Streptococcus pneumoniae*. **Aerobic and facultative gram-negative microorganisms:** *Haemophilus influenzae*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*.

INDICATIONS AND USAGE: CIPRODEX[®] Otic is indicated for the treatment of infections caused by susceptible isolates of the designated microorganisms in the specific conditions listed below: **Acute Otitis Media** in pediatric patients (age 6 months and older) with tympanostomy tubes due to *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Pseudomonas aeruginosa*. **Acute Otitis Externa** in pediatric (age 6 months and older), adult and elderly patients due to *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

CONTRAINDICATIONS

CIPRODEX[®] Otic is contraindicated in patients with a history of hypersensitivity to ciprofloxacin, to other quinolones, or to any of the components in this medication. Use of this product is contraindicated in viral infections of the external canal including herpes simplex infections.

WARNINGS

FOR OTIC USE ONLY (This product is not approved for ophthalmic use.) **NOT FOR INJECTION**

CIPRODEX[®] Otic should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolones. Serious acute hypersensitivity reactions may require immediate emergency treatment.

PRECAUTIONS

General: As with other antibacterial preparations, use of this product may result in overgrowth of nonsusceptible organisms, including yeast and fungi. If the infection is not improved after one week of treatment, cultures should be obtained to guide further treatment. If otitis persists after a full course of therapy, or if two or more episodes of otitis occur within six months, further evaluation is recommended to exclude an underlying condition such as cholesteatoma, foreign body, or a tumor. The systemic administration of quinolones, including ciprofloxacin at doses much higher than given or absorbed by the otic route, has led to lesions or erosions of the cartilage in weight-bearing joints and other signs of arthropathy in immature animals of various species. Guinea pigs dosed in the middle ear with CIPRODEX[®] Otic for one month exhibited no drug-related structural or functional changes of the cochlear hair cells and no lesions in the ossicles. CIPRODEX[®] Otic was also shown to lack dermal sensitizing potential in the guinea pig when tested according to the method of Buehler. No signs of local irritation were found when CIPRODEX[®] Otic was applied topically in the rabbit eye. **Information for Patients:** For otic use only. (This product is not approved for use in the eye.) Warm the bottle in your hand for one to two minutes prior to use and shake well immediately before using. Avoid contaminating the tip with material from the ear, fingers, or other sources. Protect from light. If rash or allergic reaction occurs, discontinue use immediately and contact your physician. It is very important to use the ear drops for as long as the doctor has instructed, even if the symptoms improve. Discard unused portion after therapy is completed. **Acute Otitis Media in pediatric patients with tympanostomy tubes:** Prior to administration of CIPRODEX[®] Otic in patients (6 months and older) with acute otitis media through tympanostomy tubes, the solution should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness which may result from the instillation of a cold solution. The patient should lie with the affected ear upward, and then the drops should be instilled. The tragus should then be pumped 5 times by pushing inward to facilitate penetration of the drops into the middle ear. This position should be maintained for 60 seconds. Repeat, if necessary, for the opposite ear (see **DOSAGE AND ADMINISTRATION**). **Acute Otitis Externa:** Prior to administration of CIPRODEX[®] Otic in patients with acute otitis externa, the solution should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness which may result from the instillation of a cold solution. The patient should lie with the affected ear upward, and then the drops should be instilled. This position should be maintained for 60 seconds to facilitate penetration of the drops into the ear canal. Repeat, if necessary, for the opposite ear (see **DOSAGE AND ADMINISTRATION**).

Drug Interactions: Specific drug interaction studies have not been conducted with CIPRODEX[®] Otic. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** Long-term carcinogenicity studies in mice and rats have been completed for ciprofloxacin. After daily oral doses of 750 mg/kg (mice) and 250 mg/kg (rats) were administered for up to 2 years, there was no evidence that ciprofloxacin had any carcinogenic or tumorigenic effects in these species. No long term studies of CIPRODEX[®] Otic have been performed to evaluate carcinogenic potential. Eight *in vitro* mutagenicity tests have been conducted with ciprofloxacin, and the test results are listed below: *Salmonella*/Microsome Test (Negative), *E. coli* DNA Repair Assay (Negative), Mouse Lymphoma Cell Forward Mutation Assay (Positive), Chinese Hamster V79 Cell HGPRT Test (Negative), Syrian Hamster Embryo Cell Transformation Assay (Negative), *Saccharomyces cerevisiae* Point Mutation Assay (Negative), *Saccharomyces cerevisiae* Mitotic Crossover and Gene Conversion Assay (Negative), Rat Hepatocyte DNA Repair Assay (Positive). Thus, 2 of the 8 tests were positive, but results of the following 3 *in vivo* test systems gave negative results: Rat Hepatocyte DNA Repair Assay, Micronucleus Test (Mice), Dominant Lethal Test (Mice). Fertility studies performed in rats at oral doses of ciprofloxacin up to 100 mg/kg/day revealed no evidence of impairment. This would be over 100 times the maximum recommended clinical dose of otic ciprofloxacin based upon body surface area, assuming total absorption of ciprofloxacin from the ear of a patient treated with CIPRODEX[®] Otic twice per day according to label directions. Long term studies have not been performed to evaluate the carcinogenic potential of topical otic dexamethasone. Dexamethasone has been tested for *in vitro* and *in vivo* genotoxic potential and shown to be positive in the following assays: chromosomal aberrations, sister-chromatid exchange in human lymphocytes and micronuclei and sister-chromatid exchanges in mouse bone marrow. However, the Ames/Salmonella assay, both with and without S9 mix, did not show any increase in His⁺ revertants. The effect of dexamethasone on fertility has not been investigated following topical otic application. However, the lowest toxic dose of dexamethasone identified following topical dermal application was 1.802 mg/kg in a 26-week study in male rats and resulted in changes to the testes, epididymis, sperm duct, prostate, seminal vesicle, Cowper's gland and accessory glands. The relevance of this study for short term topical otic use is unknown.

Pregnancy

Teratogenic Effects. Pregnancy Category C: Reproduction studies have been performed in rats and mice using oral doses of up to 100 mg/kg and IV doses up to 30 mg/kg and have revealed no evidence of harm to the fetus as a result of ciprofloxacin. In rabbits, ciprofloxacin (30 and 100 mg/kg orally) produced gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion, but no teratogenicity was observed at either dose. After intravenous administration of doses up to 20 mg/kg, no maternal toxicity was produced in the rabbit, and no embryotoxicity or teratogenicity was observed. Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. Animal reproduction studies have not been conducted with CIPRODEX[®] Otic. No adequate and well controlled studies have been performed in pregnant women. Caution should be exercised when CIPRODEX[®] Otic is used by a pregnant woman.

Nursing Mothers: Ciprofloxacin and corticosteroids, as a class, appear in milk following oral administration. Dexamethasone in breast milk could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical otic administration of ciprofloxacin or dexamethasone could result in sufficient systemic absorption to produce detectable quantities in human milk. Because of the potential for unwanted effects in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: The safety and efficacy of CIPRODEX[®] Otic have been established in pediatric patients 6 months and older (837 patients) in adequate and well-controlled clinical trials. Although no data are available on patients less than age 6 months, there are no known safety concerns or differences in the disease process in this population that would preclude use of this product. (See **DOSAGE AND ADMINISTRATION**.) No clinically relevant changes in hearing function were observed in 69 pediatric patients (age 4 to 12 years) treated with CIPRODEX[®] Otic and tested for audiometric parameters.

ADVERSE REACTIONS

In Phases II and III clinical trials, a total of 937 patients were treated with CIPRODEX[®] Otic. This included 400 patients with acute otitis media with tympanostomy tubes and 537 patients with acute otitis externa. The reported treatment-related adverse events are listed below:

Acute Otitis Media in pediatric patients with tympanostomy tubes: The following treatment-related adverse events occurred in 0.5% or more of the patients with non-intact tympanic membranes.

Adverse Event	Incidence (N=400)
Ear discomfort	3.0%
Ear pain	2.3%
Ear precipitate (residue)	0.5%
Irritability	0.5%
Taste perversion	0.5%

The following treatment-related adverse events were each reported in a single patient: tympanostomy tube blockage; ear pruritus; tinnitus; oral moniliasis; crying; dizziness; and erythema. **Acute Otitis Externa:** The following treatment-related adverse events occurred in 0.4% or more of the patients with intact tympanic membranes.

Adverse Event	Incidence (N=537)
Ear pruritus	1.5%
Ear debris	0.6%
Superimposed ear infection	0.6%
Ear congestion	0.4%
Ear pain	0.4%
Erythema	0.4%

The following treatment-related adverse events were each reported in a single patient: ear discomfort; decreased hearing; and ear disorder (tingling).

DOSAGE AND ADMINISTRATION

CIPRODEX[®] Otic SHOULD BE SHAKEN WELL IMMEDIATELY BEFORE USE

CIPRODEX[®] Otic contains 3 mg/mL (3000 µg/mL) ciprofloxacin and 1 mg/mL dexamethasone.

Acute Otitis Media in pediatric patients with tympanostomy tubes: The recommended dosage regimen for the treatment of acute otitis media in pediatric patients (age 6 months and older) through tympanostomy tubes is: Four drops (0.14 mL, 0.42 mg ciprofloxacin, 0.14 mg dexamethasone) instilled into the affected ear twice daily for seven days. The solution should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness, which may result from the instillation of a cold solution. The patient should lie with the affected ear upward, and then the drops should be instilled. The tragus should then be pumped 5 times by pushing inward to facilitate penetration of the drops into the middle ear. This position should be maintained for 60 seconds. Repeat, if necessary, for the opposite ear. Discard unused portion after therapy is completed. **Acute Otitis Externa:** The recommended dosage regimen for the treatment of acute otitis externa is: For patients (age 6 months and older): Four drops (0.14 mL, 0.42 mg ciprofloxacin, 0.14 mg dexamethasone) instilled into the affected ear twice daily for seven days. The solution should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness, which may result from the instillation of a cold solution. The patient should lie with the affected ear upward, and then the drops should be instilled. This position should be maintained for 60 seconds to facilitate penetration of the drops into the ear canal. Repeat, if necessary, for the opposite ear. Discard unused portion after therapy is completed.

HOW SUPPLIED

CIPRODEX[®] (ciprofloxacin 0.3% and dexamethasone 0.1%) Sterile Otic Suspension is supplied as follows: 5 mL fill and 7.5 mL fill in a DROP-TAINER[®] system. The DROP-TAINER[®] system consists of a natural polyethylene bottle and natural plug, with a white polypropylene closure. Tamper evidence is provided with a shrink band around the closure and neck area of the package. NDC 0065-8533-01, 5 mL fill; NDC 0065-8533-02, 7.5 mL fill. Storage: Store at controlled room temperature, 15°C to 30°C (59°F to 86°F). Avoid freezing. Protect from light.

Clinical Studies: In a randomized, multicenter, controlled clinical trial, CIPRODEX[®] Otic dosed 2 times per day for 7 days demonstrated clinical cures in the per protocol analysis in 86% of AOMT patients compared to 79% for ofloxacin solution, 0.3%, dosed 2 times per day for 10 days. Among culture positive patients, clinical cures were 90% for CIPRODEX[®] Otic compared to 79% for ofloxacin solution, 0.3%. Microbiological eradication rates for these patients in the same clinical trial were 91% for CIPRODEX[®] Otic compared to 82% for ofloxacin solution, 0.3%. In 2 randomized multicenter, controlled clinical trials, CIPRODEX[®] Otic dosed 2 times per day for 7 days demonstrated clinical cures in 87% and 94% of per protocol evaluable AOE patients, respectively, compared to 84% and 89%, respectively, for otic suspension containing neomycin 0.35%, polymyxin B 10,000 IU/mL, and hydrocortisone 1.0% (neo/poly/HC). Among culture positive patients clinical cures were 86% and 92% for CIPRODEX[®] Otic compared to 84% and 89%, respectively, for neo/poly/HC. Microbiological eradication rates for these patients in the same clinical trials were 86% and 92% for CIPRODEX[®] Otic compared to 85% and 85%, respectively, for neo/poly/HC.

References:

- CIPRODEX[®] Otic package insert.
- Walters Kluever, Source Prescriber; for the year ending December 2005.
- Roland PS, Pien FD, Schultz CC, et al. Efficacy and safety of topical ciprofloxacin/dexamethasone versus neomycin/polymyxin B/hydrocortisone for otitis externa. *Curr Med Res Opin.* 2004;20:1175-1183.
- Roland PS, Block SL, Latiolais TG, et al. A comparison of ciprofloxacin/dexamethasone and neomycin/polymyxin B/hydrocortisone for the treatment of acute otitis externa. Presented at: The American Society of Pediatric Otolaryngology meeting; May 27-30, 2005; Las Vegas, NV.
- Campoli-Richards DM, Monk JP, Price A, Benfield P, Todd PA, Ward A. Ciprofloxacin: a review of its antimicrobial activity, pharmacokinetic properties and therapeutic use. *Drugs.* 1988;35:373-447.
- Loew D, Schuster O, Graul E. Dose-dependent pharmacokinetics of dexamethasone. *Eur J Clin Pharmacol.* 1986;30:225-230.

U.S. Patent Nos. 4,844,902; 6,284,804; 6,359,016

CIPRODEX[®] is a registered trademark of Bayer AG. Licensed to Alcon, Inc. by Bayer AG.

Manufactured by Alcon Laboratories, Inc.

Rx Only

Revision date: 17 July 2003

©2006 Alcon, Inc. 4/06

Alcon[®]
ALCON LABORATORIES, INC.
Fort Worth, Texas 76134
www.ciprodex.com

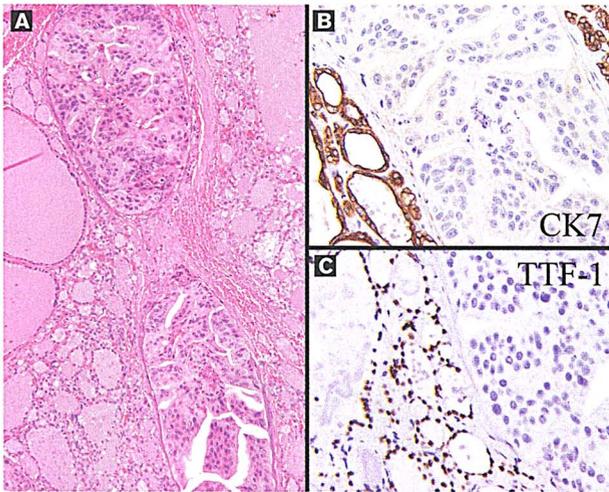


Figure 2. A: Vessels are expanded by a metastatic adenocarcinoma from a breast primary; the architecture and nuclei are unlike the adenomatoid nodules in the background (A). CK7 (B) and TTF-1 (C) highlight the thyroid parenchyma but not the metastatic breast carcinoma.

separation between primary and metastatic tumors; primary thyroid follicular tumors will usually be immunoreactive with thyroglobulin, CK7, and TTF-1, while C-cell-derived tumors will be reactive to calcitonin and chromogranin. With incredibly rare exception, metastatic tumors will not be thyroglobulin-reactive.

The prognosis of a patient with a tumor metastatic to the thyroid is determined by the underlying primary, but in most cases it is poor. However, if metastatic disease is limited to the thyroid gland, surgery can prolong survival.

Suggested reading

DeLellis R. Secondary tumours of the thyroid. In: DeLellis RA, Lloyd R, Heitz PU, Eng C, eds. Pathology and Genetics of Tumours of the Endocrine Organs and Paraganglia. Kleihues P, Sobin LH, series eds. World Health Organization Classification of Tumours. Lyon, France: IARC Press, 2004:122-3.

Heffess CS, Wenig BM, Thompson LDR. Metastatic renal cell carcinoma to the thyroid gland: A clinicopathologic study of 36 cases. Cancer 2002;95:1869-78.

Recommended by over 1,000 ENTs

CLINICAL STUDIES HAVE SHOWN BOTH GINKGO BILOBA EXTRACT AND CHELATED ZINC EFFECTIVE IN REDUCING TINNITUS.

- » Hostein N. Ginkgo special extract EGb 761 in tinnitus therapy. A survey of results of completed clinical trials. Fortschr Med Orig. 11;118(4):157-64, 2001 Jan. Review.
- » Meyer B. Multicenter randomized double-blind drug vs. placebo study of the treatment of tinnitus with Ginkgo biloba extract. Presse Med. 15(31):1562-4, 1986 Sep 25.
- » Morgenstern C, Biermann E. The efficacy of Ginkgo special extract EGb 761 in patients with tinnitus. Int J Clin Pharmacol Ther. 40(5):188-97, 2002 May.
- » Arda HN, et al. The role of zinc in the treatment of tinnitus. Otol Neurotol. 24(1):86-9, 2003 Jan.



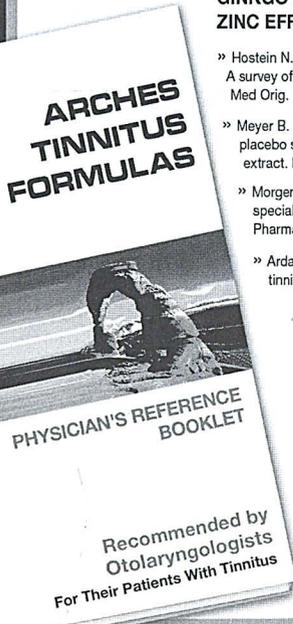
ARCHES TINNITUS RELIEF FORMULA®

MICHAEL SEIDMAN, MD, FACS

authority on tinnitus and conditions of the inner ear states:

"IT HAS BEEN MY EXPERIENCE in treating tinnitus with Arches Tinnitus Relief Formula that 10% enjoy a complete reduction of symptoms, 10% experience no change, and 80% receive some degree of relief from their symptoms, varying by individual. I recommend Arches Tinnitus Relief Formula to many of my patients* and advise them to take two capsules in the morning and again in the evening and continue this dosage for 100 days before determining the degree of relief Arches Tinnitus Relief Formula will provide."

Dr. Seidman is the Medical Director of Arches and has a small financial interest in the company.



TINNITUS RELIEF IS UNDER THE ARCH

CALL FOR A FREE PHYSICIAN'S BOOKLET PLUS CD WITH 35 CLINICAL STUDIES, C OF A, & MORE...

Visit us at
AAO-HNSF
Booth #836

TOLL FREE 800-350-9631

email: admin@archesnp.com www.tinnitusformula.com



Arches Tinnitus Formulas

*Certain people should exercise caution before taking Ginkgo biloba extract. Those taking prescription anticoagulants should consult their physician before use. Discontinue use two weeks prior to any surgical procedure.

