

T: (503) 248-9985 • TF: (800) 634-8978 • F: (503) 248-0024



Ototoxic Drug Information

The American Tinnitus Association is pleased to share several avenues where tinnitus patients can learn more about medications and tinnitus. Some prescription and over-the-counter drugs can affect/worsen existing tinnitus or, in some cases, cause tinnitus as a side effect.

In this packet is information on ototoxic drugs, including the latest copy of the PDR Drug Interaction Guide index for your reference. Also attached are some informative pieces that discuss ototoxic medications.

Before you consider any change in your medication(s) or treatment strategy, consult with your personal physician. Ask questions, and be sure to mention other medications, supplements and vitamins you currently take. These documents are designed to be utilized as a conversation tool with your doctor.

Additional resources:

- Orugwatch.com/side-effects
- Nlm.nih.gov/medlineplus/druginformation.html
- http://www.asha.org/public/hearing/Ototoxic-Medications/
- ATA.org/store/books/ototoxic-drugs-exposed-third-edition-neil-bauman-phd

SIDE EFFECTS AND INDICATIONS FOR TINNITUS



As listed in the Physicians' Desk Reference

When taken at recommended dosages, the following prescription and over-the-counter drugs have caused tinnitus in a small percentage of patients. Note: These drugs were not specifically tested on people who already had tinnitus. More information about these listed drugs can be found in the Physicians' Desk Reference. Page numbers follow the drug names on this list. All drugs listed have a reported minimum 1% occurrence of tinnitus unless otherwise noted.

Please consult with your physician before making any changes to your medication.

Α		E	
ABELCET Injection	3111	ELDEPRYL Capsules 5 mg	3
AGGRENOX Capsules	880	EMEND Capsules [<5% occurrence]	2
ALFERON N Injection	1686	EMEND for Injection [<5% occurrence]	2
ALOXI Injection	1000	ENGERIX-B Vaccine	
ALTACE Capsules	1704	EXELON Capsules and Oral Solution	2
AMBIEN Tablets	2924	EXELON Patch	:
AMBIEN CR CIV Tablets	2929	EXFORGE Tablets	:
AMERGE Tablets	1219	EXFORGE HCT Tablets	:
ANZEMET Injection	2934	F	
ANZEMET Tablets	2937	FANAPT Tablets	:
APLENZIN Tablet Extended Release	2951	FROVA Tablets	
APRISO Extended Release Capsules	2900	FUROSEMIDE Tablets USP	:
ARICEPT Tablets	1004	G	
ASACOL Delayed Release Tablets	3360	GABITRIL Tablets	
ASACOL Delayed Release Tablets	3362	GENGRAF Capsules	
ATACAND Tablets	3455	·	:
	3455 891	GEODON Capsules; GEODON Injection	
ATRIPLA Tablets			
ATRIPLA Tablets	3471	Н	
AVELOX Tablets and AVELOX I.V. Injection	1939	HYZAAR Tablets	:
В		l l	
BIAXIN FILMTAB; XL FILMTAB; GRANULES	412	IMITREX Injection	
BICILLIN C-R (King)	1712	IMITREX Nasal Spray	
BICILLIN C-R 900/300 (King)	1712	IMITREX Tablets	
BICILLIN L-A (King)	1712	INTRON A [<5% occurrence]	
BOTOX Injection	603	K	
BUTRANS System for Transdermal Administration	2864	KALETRA Tablets; Solution for Oral Use	
С		L	
CADUET Tablets	2778	LAMICTAL Tablets	
CAPASTAT SULFATE CAPREOMYCIN for Injection	1747	LAMICTAL XR Extended Release Tablets	
CARBATROL Extended Release Capsules	3095	LEVAQUIN Tablet, Solution for Oral Use; Injection	2
CARDIZEM Extended Release Tablets	423	LEVITRA Tablets	2
CELEBREX Capsules	3072	LEXAPRO Tablets and Oral Solution	
CHANTIX Tablets	2788	LIDODERM Patch	
CIALIS Tablets	1749	LIPITOR Tablets	2
CIPRO I.V	1965	LUPRON DEPOT-3 MONTH [<3% occurrence]	
CIPRO Tablets	1965	LYRICA CV Capsules; Oral Solution	2
CIPRO XR Tablets	1974	M	
CLINORIL Tablets [<1% occurrence]	1993	MAXALT Tablets; MAXALT-MLT Tablets	:
COARTEM Tablets	2454	MERIDIA CIV Capsules	
COMBIGAN Ophthalmic Solution	610	N	
COREG Tablets	1326	NADOLOL Tablets	:
COREG CR Extended Release Capsules	1333	NAMENDA Tablets/Oral Solution	
COZAAR Tablets	2001	NEORAL Capsules; Oral Solution	:
CYMBALTA Delayed Release Capsules	1759	NEXIUM Capsules; Granules	
D		NEXIUM I.V. for Injection	
DAPSONE Tablets	1696	NOROXIN Tablets	-
DEPAKOTE ER Tablet [<5% occurrence]	425	NORVIR Tablets; Solution for Oral Use	-
	0		
DEXILANT Delayed Release Capsules	3178	NORVIR Capsules; Oral Solution	



SIDE EFFECTS AND INDICATIONS FOR TINNITUS

As listed in the Physicians' Desk Reference

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Please consult with your physician before making any changes to your medication.

0		S	
OLEPTRO ER Tablets [<1% occurrence]	3446	SABRIL Tablets	1886
ORTHOCLONE OKT3 Sterile Solution	939	ST. JOSEPH Aspirin Tablets	1905
OXYCONTIN (OXYCODONE HCI CR) Tablets	2879	SALAGEN Tablets	1040
Р		SELEGILINE HYDROCHLORIDE Tablets	2440
PARNATE Tablets	1488	SEROQUE Tablets	735
PAROXETINE HYDROCHLORIDE CR Tablets	2418	SOLODYN Extended Release Tablets	1919
PAROXETINE HYDROCHLORIDE ER Tablets	2428	SORIATANE Capsules [<1% occurrence]	3138
PAXIL Tablets and Oral Suspension	1491	SPRYCEL Tablets [1% to 10% occurrence]	3527
PAXIL CR Controlled Release Tablets	1501	SUSTIVA Capsules and Tablets	3532
PEPCID Tablets	2228	T	
PERCOCET CII Tablets	1096	TARKA Tablets	547
PERCODAN USP CI Tablets	1099	TASIGNA Capsules	2592
PRIMAXIN I.M. Injectable	2233	TEKAMLO Tablets	2598
PRIMAXIN I.V. Injection	2236	TEVETEN Tablets	552
PRINIVIL Tablets	2241	TEVETEN HCT Tablets	554
PRINZIDE Tablets	2246	TOBI Nebulizer Solution [<3% occurrence]	2613
PRISTIQ Extended Release Tablets	3409	TOPROL-XL Tablets	724
PROMETRIUM Capsules	3177	TREXIMET Tablets	1578
PROVENTIL Inhalation Aerosol	2268	TRICOR Tablets	558
PYLERA Capsules	788	TRISENOX Injection [5% occurrence]	983
R		U	
RANEXA Tablets Extended Release	1168	ULORIC Tablets	3194
REMERON Tablets	2282	V	
REMERONSolTab Tablets	2286	VIAGRA Tablets	2823
REQUIP Tablets	1527	VICOPROFEN CIII Tablets	578
RESCRIPTOR Tablets	3313	VIMPAT CV Tablet; Injection	3265
RISPERDAL CONSTA Long Acting Injection	2741	W	
RYTHMOL Tablets	1545	WELLBUTRIN Tablets	1615
RYTHMOL SR Extended Release Capsules	1549	WELLBUTRIN SR Tablets [6% occurrence]	1621
		Х	
		XIFAXAN Tablets	2911
		XYREM Oral Solution [<5% occurrence]	2951

Ototoxic Medications

Drugs that can cause hearing loss and tinnitus



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his pamphlet indicates which most commonly used medications could potentially cause damage to your hearing, or aggravate an already existing problem. It is important that you, the patient, take responsibility in knowing which drugs you should try to avoid. Usually any hearing problem will only be caused by exceeding the recommended dosage of the medications. Often these problems are reversible upon discontinuation of the drug. Occasionally there are times when this change in hearing can be permanent. If you are experiencing a hearing problem, or if there is a hearing disorder in your family, it is imperative that your treating physician and pharmacist be aware of this fact. If you are prescribed one of the medications found on this list, you should speak to your physician to see if another, potentially less toxic drug, could be used in its place. If the drug is over-the-counter, you should ask the pharmacist for a recommendation of a less toxic drug.

In the lists that follow, the generic name of the drug is given first, with the trade name, if available, followed in parentheses and capitalized. Many times a particular generic drug is manufactured under several trade names.

Orin S. Kaufman, D.O.

The trade names mentioned in this article were selected by the author randomly. The inclusion of a particular trade name and the exclusion of another should not be interpreted as prejudicial either for one nor against the other.

Drugs that can cause hearing loss

Salicylates

- aspirin and aspirincontaining products
- salicylates and methylsalicylates (*linaments*)

(Toxic effects appear to be dose related and are almost always reversible once medications are discontinued.)

Non-Steroidal Anti-Inflammatory Drugs (NSAIDS)

(Most NSAIDS have the potential for causing hearing loss and/or tinnitus. Because new drugs are being frequently approved for use, it is important that you check with your doctor or pharmacist to determine if the drug you were prescribed can cause a problem.)

- diclofenac (Voltaren)
- etocolac (Lodine)
- fenprofen (Nalfon)
- ibuprofen (Motrin, Advil, Nuprin, etc.)
- indomethacin (Indocin)
- naproxen (Naprosyn, Anaprox, Aleve)
- piroxicam (Feldene)
- sulindac (Clinoril)

(Toxic effects are dose related and are almost always reversible once medications are discontinued.)

Antibiotics

- aminoglycosides
 - amikacin (Amakin)
 - gentamycin (Garamycin)
 - kanamycin (Kantrex)
 - neomycin (Found in many over-thecounter antibiotic ointments.)
 - netilmicin (Netromycin)
 - streptomycin
 - tobramycin (Nebcin)

(Of particular interest is that topical ear drop medications containing gentamycin or neomycin do not appear to be ototoxic in humans unless the tympanic membrane

(ear drum) is perforated. When a solution of an aminoglycoside antibiotic is used on the skin together with an aminoglycoside antibiotic used intravenously, there is a risk of an increase of the ototoxic effect, especially if the solution is used on a wound that is open or raw, or if the patient has underlying kidney damage. Neomycin is the drug that is most toxic to the structure involved in hearing, the cochlea, so it is recommended for topical use only. But even topical therapy has resulted in hearing loss when large areas were treated which allowed for large amounts of the drug to be absorbed into the body. Hearing loss caused by this class of antibiotics is usually permanent.)

- erythromycin
 - -(EES)
 - (E-mycin)
 - (Ilosone)
 - (*Eryc*)
 - (Pediazole)
 - (Biaxin)
 - (Zithromax)

(Usually ototoxic when given in intravenous doses of 2-4 grams per 24 hours, especially if there is underlying kidney failure.)

- vancomycin (Vancocin) (Similar to aminoglycosides in that it may be ototoxic when used intravenously in life-threatening infections. The fact that aminoglycosides and vancomycin are often used together intravenously when treating life-threatening infections futher exaggerates the problem.)
- minocycline (Minocin) (Similar to erythromycin)
- polymixin B & amphotericin B (Antifungal preparations)
- capreomycin (Capestat) (Anti-tuberculosis medication)

Diuretics

- bendroflumethazide (Corzide)
- bumetadine (Bumex)
- chlor-thalidone (*Tenoretic*)
- ethacrynic acid (*Edecrin*)
- furosemide (*Lasix*)

(These are usually ototoxic when given intravenously for acute kidney failure, acute hypertensive crisis, or acute pulmonary edema/congestive heart failure. Rare cases of ototoxicity have been found when these medications are taken orally in high doses by people with chronic kidney disease.)

Chemotherapeutic Agents

- bleomycine (*Blenoxane*)
- bromocriptine (Parlodel)
- carboplatinum (Carboplatin)
- cisplatin (*Platinol*)
- methotrexate (Rheumatrex)
- nitrogen mustard (Mustargen)
- vinblastin (Velban)
- vincristine (Oncovin)

(The ototoxic effects can be minimized by carefully monitoring blood levels.)

Quinine

- chloroquine phosphate (Aralen)
- quinacrine hydrochloride (*Atabrine*)
- quinine sulfate (Quinam) (The ototoxic effects are very similar to those of aspirin.)

Mucosal Protectant

misoprostol (Cytotec)

Narcotic Analgesics

• hydrocodone (Lorcet, Vicodin)

Drugs that can cause tin

Vapors, Solvents

- cyclohexane
- dichloromethane
- hexane (gasoline)
- lindane (Kwell)
- methyl-chloride
- methyl-n-butyl-ketone
- perchlor-ethylene
- Styrene
- tetrachlor-ethane
- toluol
- trichloroethylene

Antibiotics

- aminoglycosides (see previous section)
- amphotericin B
- chloramphenicol (Chloromycetin)
- minocycline (Minocin)
- polymyxine B
- sulfonamides (Septra, Bactrim)
- vancomycin (Vancocin)

Anti-neoplastics

- bleomycin (Blenoxane)
- cis-platinum (*Platinol*)
- carboplatinum (Paraplatin)
- methotrexate (Rheumatrex)
- nitrogen mustard (Mustagen)
- vinblastin (Velban)

Diuretics

- acetazolamide (Diamox)
- bumetanide (Bumex)
- bendrofluazide
- clorothalidone (Hygroton, Tenoretic)
- diapamide
- ethacrynic acid (Edecrin)
- furosemide (Lasix)
- hydrochlorthiazide (Hydrodiuril)
- methylchlorthizide (Enduron)

Cardiac Medications

- celiprolol
- flecainide (Tambocar)
- lidocaine
- metoprolol (Lopressor)
- procainamide (Pronestyl)

nitus

- propranolol (Inderal)
- quinidine (Quinaglute, Quinidex)

Psychopharmacologic Agents

- amitryptiline (Elavil)
- benzodiazepine class
 - alprazolam (Xanax)
 - clorazepate (Tranxene)
 - chlordiazepoxide (Librium)
 - diazepam (Valium)
 - flurazepam (Dalmane)
 - lorazepam (Ativan)
 - midazolam (Versed)
 - oxazepam (Serax)
 - prozepam (Centrax)
 - quazepam (Doral)
 - temazepam (Restoril)
 - triazolam (Halcion)
- bupropion (Welbutrin)
- carbamzepine (Tegretol)
- diclofensine
- doxepin (Sinequin)
- desiprimine (Norpramin)
- fluoxetin (Prozac)
- imipramine (Tofranil)
- lithium
- melitracen
- molindon (Moban)
- paroxetin
- phenelzin (Nardil)
- protriptilin (Vivactil)
- trazodon (Desyrel)
- zimeldin

Non-Steroidal Anti-inflammatory Drugs (NSAIDS)

(Please see notation for NSAIDS under "hearing loss.")

- asprin
- acematacine
- benorilate
- benoxaprofen
- carprofen
- diclofenac (Voltaren)
- diflunisal (Dolobid)
- fenoprofen (Nalfon)
- feprazon
- ibuprofen (Motrin, Advil, Nuprin)

- indomethacin (Indocin)
- isoxicam
- ketoprofen (Orudis)
- methyl salicylates (BenGay)
- naproxen (Naprosyn, Anaprox, Aleve)
- D-Penicilliamin
- phenylbutazone (Butazolidine)
- piroxicam (Feldene)
- proglumetacin
- proquazon
- rofecoxib (Vioxx)
- salicylates
- sulindac (Clinoril)
- tolmetin (Tolectin)
- zomepirac

Glucocorticosteroids

- prednisolone (*Prednisone*)
- ACTH (adrenocorticotrophic hormone) (Acthar)

Anesthetics

- bupivacain
- tetracain
- lidocaine (*Novacaine*)

Antimalarials

- chloroquine (Aralen)
- hydroxychloroquine (Plaquinil)

Others

• thalidomide (Thalomid)

Miscellaneous Toxic Substances

- alcohol
- arsenum
- caffeine
- lead
- marijuana
- nicotine
- mercury
- auronofin (gold, Ridaura)

(Ironically, several of these drugs found to cause tinnitus, are also used to treat tinnitus (e.g., amitryptiline, benzodiazepine class, carbamazapine, furosemide, lidocaine, prednisone).)

About the League

A pioneer in hearing rehabilitation, human services, and hearing conservation. The League for the Hard of Hearing, founded in 1910, is a private not-for-profit rehabilitation agency for infants, children and adults who are hard of hearing, deaf, and deaf-blind.

The mission of the League for the Hard of Hearing is to improve the quality of life for people with all degrees of hearing loss. This is accomplished by providing hearing rehabilitation and human service programs for people who are hard of hearing and deaf, and their families, regardless of age or mode of communication.

We strive to empower consumers and professionals to achieve their potential and to provide leadership to, and be the model for, disciplines that relate to hearing rehabilitation.

We promote hearing conservation and provide public education about hearing.

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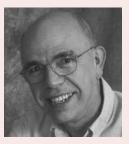
League for the Hard of Hearing 50 Broadway
New York, NY 10004
917-305-7890 Voice 917-305-7999 TTY 917-305-7888 Fax postmaster@lhh.org Email www.lhh.org URL

When Jonathan took a course of erythromycin prescribed by his doctor, the last thing on his mind was that this drug would cause him to lose his hearing in one ear, give him hyperacusis (some normal sounds seem very loud) and balance problems and result in horrific bilateral (in both ears) tinnitus.

Drugs and Tinnitus: Put Yourself in the Driver's Seat

By Neil Bauman, Ph.D.

No one warned Eunice that taking the anti-depressant drug amitriptyline (Elavil®) would result in *screaming tinnitus*, a condition much worse than her original depression. Without warning, the drugs prescribed for Jonathan (mentioned above) and Eunice to treat other health issues resulted in loud, intrusive tinnitus, making their lives almost unbearable. These stories are true, though I've changed the patients' names for this article.



Neil Bauman, Ph.D.

The author's comprehensive book, *Ototoxic Drugs Exposed,* describes the ototoxic (ear damaging) side effects of 447 drugs and 29 chemicals known to trigger tinnitus, about 300 drugs associated with hearing loss and the hundreds of drugs that affect balance and cause other ototoxic side effects. This book, as well as Dr. Bauman's *When Your Ears*

Ring (Cope with Your Tinnitus—Here's How), is available with member discount pricing in the online ATA Store at www.ata.org.

Annual Physician's Desk Reference (PDR) guides are available by contacting ATA at (800) 634-8978 x219 or lisa@ata.org.

Ototoxic Drugs—What Are They?

Ototoxic (OH-toe-TOKS-ik) drugs are those medications that can cause ototoxic (ear damaging) side effects to your ears. Such drugs can cause hearing loss, hyperacusis, tinnitus and other phantom sounds and a whole host of balance problems. This does not happen to everyone who takes drugs, by any means, but it does happen to a significant number of unfortunate people.

Note this well. Even though a drug's description lists tinnitus as a side effect, this does not mean that you will develop tinnitus if you take it. Some people do. Many don't. The problem is that you don't know into which class you will fall. Therefore, you should learn

about the side effects of any drug before you begin taking it. Be particularly cautious until you know that any given drug won't adversely affect your ears.

Which Drugs Can Cause Tinnitus?

There are more than 450 prescription and over-the-counter drugs from acebutolol (Sectral®) to zuclopen-thixol (Clopixol®) that can trigger tinnitus, make existing tinnitus worse or cause another (new) tinnitus sound to appear.

Most of the drug classes have tinnitus-causing drugs sprinkled throughout. For example, antibiotics, pain-killers, anti-anxiety and anti-depression drugs, anti-malarial medications, anti-cancer drugs and blood pressure controlling medications, to name a few, can all trigger tinnitus.

Is Drug-Induced Tinnitus Temporary or Permanent?

Tinnitus arising from taking ototoxic drugs may, or may not, be permanent. The good news is that tinnitus resulting from taking such drugs is often temporary and goes away in a few days to a few weeks after you stop taking the drug. For example, ototoxic anti-inflammatories such as acetylsalicylic acid (aspirin), ibuprofen (Advil®) and naproxen (Aleve®) generally cause temporary tinnitus. But there are no quarantees.

The bad news is that the resulting tinnitus may be permanent. For example, if you are taking an aminoglycoside antibiotic, you are lucky if the tinnitus stops within a couple of weeks after you finish the drug therapy. For a good number of people, this kind of tinnitus never goes away.

Some Drugs Produce Distinctive Tinnitus Sounds

Drug-induced tinnitus usually first appears as a continuous high-pitched sound in both ears. However,

certain ototoxic drugs produce distinctive tinnitus sounds. For example, tinnitus caused by aspirin and quinine (and related drugs) is generally a high-pitched or hissing sound, and may sound like a continuous musical note. In contrast, tinnitus caused by erythromycin can produce what sounds like "blowing," while loop diuretics (such as furosemide [Lasix®]) may produce a middlefrequency sound.

How Soon Will the Tinnitus Occur After Taking a Drug?

Tinnitus may show up very quickly after you

begin taking an ototoxic medication, or it may take several days for it to become obvious to you. For example, tinnitus from loop diuretics may start just minutes after you begin receiving them intravenously (directly into a vein). In contrast, tinnitus may not show up until two or three days after taking an aminoglycoside antibiotic. Strangely enough, with certain drugs, such as the benzodiazepines (a class of tranquilizers), tinnitus may only start after you have stopped taking the drug.

Tinnitus, Hearing Loss and Drugs

Hearing loss and tinnitus often go together. I have seen it reported that about 70 percent of people with hearing loss also have tinnitus. Therefore, if you preserve your hearing, you can help yourself avoid unnecessary tinnitus. To this end, you should be aware that there are around 300 drugs associated with hearing loss. Taking such drugs may result in both hearing loss and tinnitus.

Tinnitus often precedes or accompanies hearing loss. In fact, tinnitus is the number one indicator that you may be doing damage to your ears from an ototoxic drug. It also may be the only warning you'll ever get, so don't ignore it!

It's All About Choices— What You Can Do About Tinnitus

Knowledge is power. When you are aware of the many drugs that can damage your ears, and the many risk factors that can make you even more



Just because a drug label does not list tinnitus as a possible side effect, does not mean it will not cause tinnitus. For example, when Sarah's doctor doubled her dose of irbesartan (Avapro®), her existing tinnitus became noticeably louder. When she complained to her doctor, he reduced her dose and her tinnitus returned to its previous level. But still, irbesartan is not listed as causing tinnitus.

susceptible to ototoxic side effects, you are in a position to help protect your precious ears.

If your ears start to ring after you begin taking a new drug, or an increased dose of an existing drug, you should immediately report this to your doctor. Together, you should then decide what to do - whether to reduce the dose to a level below where it causes tinnitus, or stop taking the medication altogether and try another.

You need to decide for yourself about the trade offs to taking

any given medication. For example, Joan takes celecoxib (Celebrex®) for her arthritis. When she takes it, her tinnitus gets louder, but her arthritis pain improves. She chooses the increased tinnitus (which doesn't really bother her) over the arthritis pain (which she definitely doesn't like). That is her choice, and she is content to live with it.

Harold, on the other hand, began taking amitriptyline and soon noticed he had severe tinnitus. As he says, his tinnitus was driving him "buggy," so he contacted me for help. I suggested the amitriptyline might be causing his tinnitus. With his doctor's permission, he stopped taking the drug. Twelve days later, he joyfully reported that his tinnitus went away. That was his choice and he is glad he made it.

When it comes to your ears, don't let ototoxic drugs flip your world upside down! Remain in the driver's seat and take control by reading, asking questions and making the best choices you can. ((

Neil Bauman, Ph.D. is the Executive Director of the Center for Hearing Loss Help. His mission is educating and helping people successfully live with their hearing losses, tinnitus and other ear conditions. Dr. Bauman is both a speaker and the author of ten books and hundreds of articles related to hearing loss.