

Appendix 1. Ototoxic medications

Medication	Resource	Additional Information
Acetazolamide ¹	M	
Acetaminophen ²	M	Toxicity in association with codeine
Amikacin ³⁻⁸	M, L, MIMED	
Aminocaproic Acid ^{P9}	M, L, PI	
Aminophylline ^{10,11}	M	
Amiodarone ¹²⁻¹⁴	L, MIMED, PI	Dizziness, incoordination, abnormal gait 4-9% (PI). 12% incidence of chronic bilateral vestibulopathy among 126 patients taking amiodarone. Vestibular symptoms sometimes fully reversible.
Amitriptyline ^{15,16}	M, L	Used for vestibular migraine
Amlodipine ¹⁷	M	Dizziness (3%)
Amphotericin B ¹⁸⁻²⁰	M	
Ampicillin ^{21,22}	M, MIMED	
Aspirin ²³⁻²⁸	M, MIMED	Hearing loss is dose-related; lower doses more likely to cause reversible hearing loss
Atropine ²⁹	M	
Azithromycin ³⁰⁻³⁴	M, MIMED	
Aztreonam ³⁵	M, MIMED	
Bacitracin ³⁶	M	
Bleomycin ³⁷	M	
Bromocriptine ³⁸	M	Dizziness >10%, indication specific
Bumetanide ^{39,40}	M, MIMED	Tinnitus 1-1.7%; Diuretics alone do not directly damage the cochlear/vestibular hair cells or the spiral or vestibular ganglion neurons in experimental animals.
Bupivacaine ⁴¹	M, MIMED	
Bupropion ^{42,43}	M	Tinnitus: 1-6%
Capreomycin ^{44,45}	M, MIMED	Vertigo <1%
Carbamazepine ^{46,47}	M	Dizziness 44%
Carboplatin ⁴⁸⁻⁵³	M, L, MIMED	Hearing loss in 1% but some report 15-82%. Ototoxicity usually occurs in patients taking other ototoxic meds; little ototoxic potential alone; toxicity is cumulative
Carvedilol ⁵⁴	M	Tinnitus <1%, hearing loss <0.1%, vertigo 1-3%, dizziness 2-32%; Ototoxicity occurs with or without hypotension
Ciclopirox ⁵⁵	M	
Ciprofloxacin ^{P56}	P	Tinnitus up to 1%, dizziness 1-2%
Chloramphenicol ⁵⁷	M, MIMED	Reports in case series
Chlordiazepoxide ^{P58}	MIMED	
Chlorhexidine ⁵⁹	M	
Chloroquine ^{60,61}	M	
Chlorthalidone ⁶²	M	
Cidofovir ⁶³	M, MIMED	
Cisplatin ⁶⁴⁻⁷⁰	M, L, MIMED	Incidence in children 40-60% and adults 10-31%; hearing loss is high frequency. May be dose related, cumulative, and irreversible.
Clarithromycin ^{71,72}	M	

Clindamycin ^{73,74}	M	
Codeine ^{2,75}	M	Some reports deny ototoxic side effects
Colistin/hydrocortisone/ neomycin/thonzonium ^{P76}	MIMED	
Cyclizine ⁷⁷	MIMED	
Cycloserine ^{P78}	M	Dizziness and central vertigo
Cyclosporine ^{79,80}	M, L	Risk of ototoxicity when combined with doxorubicin or cyclosporine A
Cyproheptadine ^{P81}	MIMED	
Cytarabine ^{82,83}	M	
Danazol ⁸⁴	M	
Dantrolene ⁸⁵	M	
Dapsone ⁸⁶	M	Dizziness manifests as vertigo
Dasatinib ⁸⁷	L	
Deferoxamine ⁸⁸⁻⁹¹	M	Cochleotoxicity up to 31%
Desipramine ⁹²	M	
Diazepam ⁹³	M, MIMED	
Diclofenac ⁹⁴⁻⁹⁶	M	Can cause sudden sensorineural hearing loss; dizziness manifests as vertigo
Didanosine ^{97,98}	M, MIMED	
Diflunisal ⁹⁹	M	Cochleotoxicity 1-3%
Diltiazem ^{100,101}	M	
Docetaxel ^{P102}	L	
Donepezil ¹⁰³	M	
Doxepin ^{104,105}	M	
Doxycycline ¹⁰⁶	M	
Efavirenz ^{107,108}	M	
Eflornithine ^{109,110}	MIMED	
Enalapril ¹¹¹	M, L, MIMED	Dizziness manifests as vertigo
Enalaprilat ¹¹²	M	
Erlotinib ¹¹³	M	
Erythromycin ¹¹⁴⁻¹¹⁶	M, MIMED	
Eszopiclone ^{P117}	L	
Ethacrynic Acid ¹¹⁸	M, MIMED	
Ethionamide ^{44,119}	M	Concurrent administration of pyridoxine recommended to reduce/prevent neurotoxic effects. Incidence of hearing impairment attributable to ethionamide alone is complicated by concomitant administration of other anti-TB drugs (eg, kanamycin).
Etidronate ^{120,121}	M, MIMED	Case reports of tinnitus in 2 women, however they both had otosclerosis
Etodolac ⁹⁴	M, MIMED	Tinnitus 1-3%, hearing loss <1%, dizziness 3-9%
Famotidine ¹²²	M, MIMED	Tinnitus <1%, dizziness 1%
Fenoprofen ^{94,123}	M, MIMED	Tinnitus 2-5%, dizziness 7%
Flecainide ¹²⁴	M, MIMED	Tinnitus 1-10%, vertigo 1-3%, dizziness > 10%
Fludarabine ¹²⁵	M	Hearing loss 2-6%

Fluoxetine ¹²⁶	M	Tinnitus 1-10%, otalgia 1-10%, dizziness 9%
Flurazepam ^{93,127}	MIMED	
Furosemide ^{118,128-132}	M, MIMED	Tinnitus 3-6% (PO), 50-100% (IV)
Gadoterido ^{133,134}	MIMED	Tinnitus $\leq$ 1%, hearing loss $\leq$ 1%, dizziness <1%
Gentamicin ¹³⁵⁻¹⁵¹	M, MIMED	Hearing loss is high frequency
Glycerin ¹⁵²	MIMED	
Gramicidin	MIMED	Stinging (ie, physical pain) reported in some patients treated with otic preparation
Hepatitis B vaccine ^{153,154}	M	Otalgia
Homatropine ¹⁵⁵	MIMED	
Hydrochlorothiazide ^{62,156}	M	
Hydrocodone/ acetaminophen ^{75,157,158}	M	
Hydroxychloroquine ¹⁵⁹⁻¹⁶³	M	
Hyaluronidase ^{P164}	M	
Ibuprofen ⁹⁴	M	Tinnitus $\leq$ 3%
Ifosfamide ^{165,166}	M	Tinnitus $\leq$ 1%, hearing loss $\leq$ 1%
Imipramine ¹⁶⁷⁻¹⁶⁹	M	
Indomethacin ^{94,123}	M	Tinnitus 1-3%, hearing loss $\leq$ 1%, vertigo 1-3%, dizziness 3-9%
Interferon ¹⁷⁰⁻¹⁷²	M	Otalgia ($\leq$ 5%), hearing loss (<5%), labyrinth disease (<5%), otitis media (<5%), tinnitus (<5%); some sources report incidence of cochleotoxicity up to 39.5%; dizziness $\leq$ 23%
Isoniazid ¹⁷³	M	Cochleotoxicity 16.6%
Isotretinoin ¹⁷⁴	M	
Itraconazole ¹⁷⁵	M	Tinnitus $\leq$ 2%, hearing loss $\leq$ 2%, dizziness 1.2-4%
Kanamycin ^{176,177}	M, MIMED	Hearing loss 5-26.9%
Ketoconazole ¹⁷⁸	M	Dizziness $\leq$ 1%
Ketoprofen ⁹⁴	M	Tinnitus 1-3%, dizziness $\geq$ 1%
Ketorolac ^{179,180}	M	Tinnitus 1-10%, dizziness 1-10%
Lamivudine ^{98,181,182}	M, MIMED	
Lidocaine ¹⁸³	M	Frequency not defined: Tinnitus and dizziness (per package insert); also used as treatment for tinnitus: lidocaine-induced change in tinnitus loudness
Lithium ^{184,185}	M	Frequency not defined: Tinnitus and dizziness; vertigo (per package label)
Lorazepam ⁹³	M, MIMED	Dizziness (7%), unsteadiness (3%); vertigo frequency not defined; <1% postmarketing hearing loss
Lovastatin ^{186,187}	M,	dizziness ($\leq$ 1%); little to no evidence for ototoxicity but may improve toxicity due to hyperlipidemic effects (referenced above); reduction in coq10 from statins potentially linked to tinnitus but no studies
Magnesium salicylate ¹⁸⁸	M	side effect profile similar to that of aspirin; short-term administration, the effects appear to be completely reversible whereas long-term administration appears to induce a unique form of damage to SGN (salicylates in general/extrapolated)
Mannitol ¹⁸⁹	M	dizziness frequency not defined (diuresis; package insert); often used in chemo regimens with other ototoxic agents like cisplatin; also has otoprotective properties through free radical scavenger
Measles vaccine ¹⁹⁰	MIMED	dizziness and hearing loss frequency not defined (package insert); reporting rate of hearing loss in the US after MMCV estimated at one per 6—8 million doses.
Mechlorethamine ¹⁹¹	MIMED	Otic: Deafness, tinnitus, vertigo frequency not defined (package label); very little instances of clinical hearing loss associated with doses of 0.4 mg/kg or less in literature (was more common when higher doses used years ago).

Mefenamic acid ^{23,192}	M	dizziness 3-9%; NSAID; may induce false positives for hearing loss through activation of cochlear NMDA receptors; controversial data regarding ototoxicity
Mefloquine ^{193,194}	M, L	Neuropsychiatric effects; dizziness or vertigo, tinnitus, and loss of balance may also occur and have been reported to be permanent in some cases (<1% post marketing and case reports per lexicomp / package insert); mostly cohort studies found but in package labeling (C evidence that ototoxicity may be reversible; RCT where hearing loss or tinnitus not observed..RCT tinnitus observed)
Meningococcal Diphtheria Vaccine ¹⁹⁵	L	<1% post marketing dizziness, equilibrium disturbance, vertigo. (Menactra/ Menveo ACWY).
Meprobamate/Aspirin ¹⁹⁶	MIMED	package insert dizziness vertigo frequency not defined for meprobamate alone
Methylergonovine ¹⁹⁷	M	tinnitus and dizziness frequency not defined
Metronidazole ¹⁹⁸	M, MIMED	dizziness (4%); frequency not defined for vertigo.
Minocycline ¹⁹⁹⁻²⁰¹	M, MIMED	Dizziness (9%); tinnitus (2%), <1% post marketing hearing loss; vertigo 14-60%; also shown to have protective effects.
Minoxidil ²⁰²	M	
Mirtazapine ²⁰³	M	Dizziness (7%); >1% vertigo; <1% post marketing deafness; has been studied for treatment of tinnitus
Misoprostol ²⁰⁴	M	<1% post marketing and or case reports of dizziness, deafness, tinnitus; literature support for treatment for tinnitus.
Moxifloxacin ²⁰⁵⁻²⁰⁷	M	dizziness (3%); <1%, post marketing, and/or case reports for vertigo and tinnitus
Mumps virus vaccine ^{P208}	MIMED	hearing loss very rare; dizziness frequency not defined; otitis media
Muromonab CD3 ²⁰⁹	M, MIMED	dizziness 6%, <1% hearing loss, vertigo, tinnitus.
Nabumetone ²¹⁰	M	Dizziness and tinnitus (3% to 9% per package insert); <1%, post marketing, and/or case reports vertigo; scattered case reports may not always be reversible
Naproxen ^{123,211,212}	M, MIMED	Dizziness (≤9%) vertigo (<3%) Tinnitus (3% to 9%), auditory disturbance (<3%).
Neomycin ²¹³⁻²¹⁶	M, L, MIMED	BBW; <1%, post marketing, and/or case reports: Auditory ototoxicity, neurotoxicity, vestibular ototoxicity. More cochleotoxic generally; often delayed in onset. Much of the well documented research has been conducted in animals
Nicardipine ^{17,217,218}	M	dizziness (4% to 7%); <1% post marketing tinnitus, vertigo; ear disorder "not associated with ototoxicity"
Nicotine ²¹⁹⁻²²²	M	dizziness frequency not defined; induces dose-dependent hair cell toxicity in embryos by promoting apoptosis and mitochondrial and structural damage in zebrafish; package insert recommends monitoring for disturbed hearing
Nifedipine ^{100,217}	M	Dizziness (10% to 27%); equilibrium disturbance (≤2%); <1%, post marketing and/or case reports of tinnitus
Nimodipine ^{100,217}	M	efficacy of nimodipine is documented in the medical management of peripheral vestibular vertigo, sensorineural hearing loss and tinnitus, even in a pathology as complex as Ménière's disease; <1%, post marketing and/or case report of dizziness.
Nitroprusside ^{223,224}	M	Data from studies in guinea pigs
Norfloxacin ²²⁵	M, MIMED	Dizziness (2% to 3%); tinnitus and hearing loss <0.3% post marketing
Nortriptyline ^{92,226}	M, MIMED	RCT exists in use for resolution of tinnitus; dizziness, tinnitus frequency not defined in package insert;
Omeprazole ²²⁷	M	dizziness in 1.5% in clinical trial. Vertigo post-market report, unknown frequency. Tinnitus in <1% post-market
Oxaliplatin ²²⁸⁻²³⁰	P	dizziness in 7% in clinical trial
Oxaprozin ²³¹⁻²³³	M	dizziness in 1-10% in trial, tinnitus in 1-10%
Oxazepam ²³⁴	MIMED	1 patient with vertigo in a trial also had cervical syndrome
Paclitaxel ²³⁵⁻²³⁷	M, L	ototoxicity in mouse study. Post-market report of hearing loss
Pamidronate ^{121,238-243}	M	2 patients with gait disturbance and imbalance categorized as vertigo
Pancuronium ²⁴⁴	M	sensorineural hearing loss reported in neonates only

Paromomycin ²⁴⁵⁻²⁴⁹	M, L	post market <1% vertigo, reversible hearing loss in 1.4% in trial, 6.7% dizziness in retrospective studies
Pembrolizumab ²⁵⁰⁻²⁵³	PI	
Phenobarbital ²⁵⁴⁻²⁵⁸	M	vertigo reported only in package insert
Phenytoin ^{255,259-261}	M	
Piroxicam ^{262,263}	M	tinnitus 1-10% in trial, hearing loss <1% post market, dizziness 1-10% in trial
Plazomicin ^{P264}	L, MIMED	2% ototoxicity, irreversible tinnitus, <1% vertigo post-market, dizziness 21%
Polymyxin B ²⁶⁵⁻²⁶⁸	M	IV formulation only
Potassium iodide ^{269,270}	M	
Prazosin ²⁷¹	M	<1% tinnitus post market, 1-4% vertigo, 10% dizziness
Prednisolone	M	Package insert only
Primaquine ^{272,273}	M	tinnitus in treatment along with other meds usually
Promethazine ^{P274}	M	tinnitus and dizziness reported in clinical trials
Propylthiouracil ²⁷⁵⁻²⁷⁸	M, MIMED	vertigo reported only in package insert
Quinidine ²⁷⁹⁻²⁸¹	M	tinnitus, hearing loss, and vertigo <1% post market, dizziness 3-15% trial, hearing loss in randomized study
Quinine ^{282,283}	M, MIMED	
Ramipril ²⁸⁴	M	tinnitus <1% post market. vertigo <2%, dizziness 2-4% in trial
Rasagiline ^{P285}	L	2% vertigo, 7% dizziness in trial
Rifampin ^{119,286}	M	dizziness in trial
Riluzole ²⁸⁷	L	2% vertigo, 4% dizziness in trial
Rimantadine ^{288,289}	M	<1% tinnitus post market, 1-2% dizziness in trial
Ritonavir ^{P290}	M	3-16% dizziness. tinnitus vertigo and hearing loss <2% in trial and package label
Rubella virus live vaccine ^{291,292}	MIMED	dizziness reported in package insert, hearing loss and vertigo in case reports
Sertraline ^{92,293-296}	M	
Sildenafil ¹²⁹⁷⁻³⁰⁰	M	tinnitus in randomized trial 2.9%, dizziness 7.7%, case report of hearing loss
Stavudine ^{98,181}	M, MIMED	ototoxic but usually given together with other drugs in highly active antiretroviral therapy (HAART)
Streptomycin ³⁰¹⁻³⁰⁴	M, L, MIMED	
Sulfamethoxazole ³⁰⁵	MIMED	Most studies examine sulfamethoxazole as combined trimethoprim-sulfamethoxazole
Sulfasalazine ³⁰⁶	M	Hearing loss reported with other similar sulfonamides e.g. azulfidine
Sulindac ^{94,123}	M	1% to 3% tinnitus, 3% to 9% dizziness
Tacrolimus ³⁰⁷⁻³⁰⁹	M	Hearing loss < 15%, dizziness 19% in clinical trials
Teicoplanin ^{310,311}	L, MIMED, PI	Incidence of ototoxicity unknown. Monitoring of auditory function recommended. Mechanism of action similar to vancomycin
Temazepam ^{93,312}	M	1.2% vertigo and 4.5% dizziness in controlled trial
Telmisartan ^{17,313}	M	
Terazosin ^{314,315}	M	
Tetanus toxoid ³¹⁶	MIMED	
Tetracaine ³¹⁷	M	
Tetracycline ^{74,199,200}	M	
Thalidomide ³¹⁸⁻³²¹	M	
Ticlopidine ³²²	M, MIMED	
Timolol ^{323,324}	M	1% to 5% dizziness in trials

Tobramycin ^{325,326}	M, L, MIMED	10% hearing loss in cystic fibrosis patients with Pseudomonas trial
Tolmetin ⁹⁴	M	Tinnitus < 3% and dizziness 3-9% in clinical trials
Topiramate ³²⁷	M	Dizziness 4-20% in clinical trials
Torsemide ^{118,128,129,328}	M	
Tranlycypromine ³²⁹	M	Dizziness > 30% in clinical trials
Trazodone ^{P330}	M	Hearing loss < 1%, vertigo < 1%, dizziness 25% in clinical trials
Trimeprazine ³³¹	MIMED	
Valproic acid ^{255,332}	M	Hearing loss 1-5%, tinnitus 1-7%, dizziness 12-25% in clinical trial
Valsartan ³³³	M	Dizziness 2-17% in clinical trial
Vancomycin ³³⁴⁻³³⁷	M, L, MIMED	
Venlafaxine ^{92,338}	M	Dizziness 11-23.9% in clinical trials
Verapamil ²¹⁷	M	Dizziness 3-5% in clinical trials
Vigabatrin ^{P339}	MIMED	Tinnitus 2% clinical trial, vertigo 2% in complex partial seizures, dizziness 24% in complex partial seizures
Vinblastine ^{340,341}	M	
Vincristine ^{342,343}	M, MIMED	
Vinorelbine ³⁴⁴	L, MIMED	
Vitamin D ³⁴⁵	M	There are reports that vitamin D improves vestibular symptoms
Zidovudine ^{98,181,346}	M, MIMED	

Abbreviations: L (Lexicomp), M (Miller et al.)³⁴⁷, MIMED (Micromedex), PI/P (package insert), RCT randomized controlled trial

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