Drugs With Anticholinergic Activity

Drugs with anticholinergic activity increase the risk of adverse effects (e.g., delirium, cognitive impairment, dry mouth, constipation, falls), especially in the elderly.[1,6,10] They can also interact with other drugs to reduce their effectiveness or further increase the risk of adverse effects.[2] Anticholinergics have different adverse and clinical effects based on their affinity for the different muscarinic receptors and their ability to cross the blood-brain barrier.[7] Prolonged use of medium/high activity anticholinergics is associated with dementia, but is not definitively causative.[9,11,12] When deprescribing anticholinergics, consider stopping or lowering the dose of the med with the highest anticholinergic activity first (when possible), or switch to lower anticholinergic activity meds. The chart below groups drugs by anticholinergic activity.[a] To help you optimize drug use in the elderly, and for **therapeutic alternatives** for problematic drugs, see our chart, *Potentially Harmful Drugs in the Elderly: Beers List*. In addition, our *Natural Medicines* has a list of supplements that have anticholinergic activity.

This chart may not include all drugs with anticholinergic activity.

Drugs with Potential Anticholinergic Activity		
Drug Class	**MEDIUM/HIGH Activity**[1,3,4,5,8,a]	**LOW Activity**[1,3,4,8,a]
Analgesics	Meperidine Tramadol	Celecoxib Codeine Fentanyl Morphine Oxycodone
Antibiotics	None	Ampicillin Cefoxitin Clindamycin Cycloserine (*Seromycin*)-US only Gentamicin Piperacillin Vancomycin
Anticonvulsants	Carbamazepine Oxcarbazepine	Valproic Acid

Drugs with Potential Anticholinergic Activity		
Drug Class	**MEDIUM/HIGH Activity**[1,3,4,5,8,a]	**LOW Activity**[1,3,4,8,a]
Antidepressants	Amitriptyline Amoxapine-US only Clomipramine Desipramine Doxepin >6 mg Imipramine Nortriptyline Paroxetine Protriptyline-US only Trimipramine	Bupropion Citalopram Escitalopram Fluoxetine Fluvoxamine Mirtazapine Sertraline Trazodone Venlafaxine
Antihistamines	Brompheniramine Carbinoxamine-US only Cetirizine (controversial) Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Diphenhydramine Doxylamine Fexofenadine (controversial) Hydroxyzine Pyrilamine Triprolidine	Desloratadine Levocetirizine Loratadine
Antimuscarinics (Overactive Bladder Agents)	Darifenacin (*Enablex*) Fesoterodine (*Toviaz*) Flavoxate Oxybutynin (*Ditropan*) Propiverine-Canada only Solifenacin (*Vesicare*) Tolterodine (*Detrol*) Trospium	None The extent of anticholinergic side effects seen with antimuscarinics will vary depending on the formulation used (e.g., immediate-release vs long-acting or topical). CNS effects depend on the extent of CNS penetration and the drug's affinity to M1 receptors in the brain. See our chart, *Medications for Overactive Bladder*, for a comparison of these drugs.

Drugs with Potential Anticholinergic Activity		
Drug Class	**MEDIUM/HIGH Activity**[1,3,4,5,8,a]	**LOW Activity**[1,3,4,8,a]
Anti-Parkinson Agents	Amantadine Benztropine Trihexyphenidyl	Bromocriptine Carbidopa/Levodopa Entacapone (*Comtan*) Pramipexole (*Mirapex*) Phenelzine (*Nardil*) Selegiline
Antipsychotics	Chlorpromazine Clomipramine Clozapine Fluphenazine Haloperidol Loxapine Methotrimeprazine (Canada) Olanzapine Perphenazine Pimozide Quetiapine Thioridazine-US only Thiothixene-US only Trifluoperazine	Aripiprazole Asenapine Iloperidone-US only Paliperidone Risperidone Ziprasidone
Benzodiazepines	None	Alprazolam Chlordiazepoxide Clonazepam Clorazepate Diazepam Estazolam-US only Flurazepam Lorazepam Midazolam Oxazepam Temazepam Triazolam

Drugs with Potential Anticholinergic Activity		
Drug Class	**MEDIUM/HIGH Activity**[1,3,4,5,8,a]	**LOW Activity**[1,3,4,8,a]
Cardiovascular Agents	Disopyramide	Atenolol Captopril Chlorthalidone Digoxin Diltiazem Dipyridamole Furosemide Hydralazine Isosorbide Metoprolol Nifedipine Quinidine Triamterene Warfarin
Gastrointestinal Agents	Atropine Belladonna Dicyclomine Dimenhydrinate Homatropine Hyoscyamine Loperamide Meclizine-US only Methscopolamine-US only Prochlorperazine Promethazine Propantheline-US only Ranitidine-Canada only Scopolamine	Bisacodyl Cimetidine Clidinium Domperidone-Canada only Famotidine Metoclopramide Nizatidine
Immunosuppressants	None	Azathioprine (*Imuran*) Cyclosporine Hydrocortisone Methylprednisolone Prednisone

Drugs with Potential Anticholinergic Activity		
Drug Class	**MEDIUM/HIGH Activity**[1,3,4,5,8,a]	**LOW Activity**[1,3,4,8,a]
Muscle Relaxants	Baclofen Carisoprodol-US only Cyclobenzaprine Methocarbamol Orphenadrine Tizanidine	Pancuronium
Respiratory Meds	Pseudoephedrine Theophylline	Fluticasone/Salmeterol (*Advair*)
Other	None	Colchicine (*Colcrys*-US) Ketotifen Ophthalmic Lithium Metformin Methotrexate Naratriptan Sumatriptan Zolmitriptan

a. Drugs in the "MEDIUM/HIGH Activity" column are considered a "2" or "3" on at least one of the **anticholinergic scales covered below**. Drugs listed as having strong anticholinergic properties in the Beers Criteria are also in this column. "LOW Activity" drugs are not more than a "1" on any of these scales. There are a number of lists that express the degree of anticholinergic activity of different drugs, examples include:

- The **Anticholinergic Cognitive Burden List** ranks drugs as a 1 (possible [in vitro data]), 2 (definite), or 3 (definite) and is based on expert opinion and literature review. Drugs ranked as at least a 2 on this scale increase the risk of cognitive impairment by almost 50% over a period of six years.[4]
- The **Anticholinergic Risk Scale** ranks drugs on a scale of 0 (no or low risk), 1 (moderate), 2 (strong), or 3 (very strong) based on expert opinion and literature review of central and peripheral effects of drugs.[1] Scores correlate with risk of anticholinergic effects, fractures, aspiration pneumonia, and limited cognitive functional improvement after stroke.[1, -17]
- The **Anticholinergic Drug Scale** ranks drugs on a scale of 0 (no anticholinergic activity), 1 (potentially anticholinergic), 2 (anticholinergic adverse events sometimes noted), or 3 (marked anticholinergic activity) based on serum anticholinergic activity.[3] Anticholinergic Drug Scale level 2 and 3 drugs have been associated with fracture risk, and higher summative scores with mortality.[13,14]
- The **Beers Criteria** used a composite of several scales to draft a list of drugs with strong anticholinergic properties.[5] There is a ***cumulative*** dose-response relationship between use of strong anticholinergics and development of dementia.[9]
- The **Anticholinergic Load Scale** is based on previously published serum anticholinergic activity scales and expert opinion. It ranks drugs on a scale of 0 (no effect) to 3 (strong effect). Scores correlate with cognitive impairment in healthy elderly, but not those with Alzheimer's disease or mild cognitive impairment, perhaps due to the severity of their cognitive impairment or confounding by cognitive enhancers.[8]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

References

1. Rudolph JL, Salow MJ, Angelini MC, McGlinchey RE. The anticholinergic risk scale and anticholinergic adverse effects in older persons. Arch Intern Med. 2008 Mar 10;168(5):508-13.
2. Zarowitz BJ. Oral solid potassium chloride and anticholinergic medications: a new drug interaction for an old drug? Geriatr Nurs. 2006 Nov-Dec;27(6):329-33.
3. Carnahan RM, Lund BC, Perry PJ, et al. The Anticholinergic Drug Scale as a measure of drug-related anticholinergic burden: associations with serum anticholinergic activity. J Clin Pharmacol. 2006 Dec;46(12):1481-6.
4. Indianapolis Discovery Network for Dementia. Anticholinergic Cognitive Burden List. 2012. https://sharedcarebc.ca/sites/default/files/8.%20ACB_scale_-_legal_size.pdf. (Accessed August 8, 2022).
5. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694.
6. Hanlon JT, Semla TP, Schmader KE. Alternative Medications for Medications in the Use of High-Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly Quality Measures. J Am Geriatr Soc. 2015 Dec;63(12):e8-e18.
7. Chancellor M, Boone T. Anticholinergics for overactive bladder therapy: central nervous system effects. CNS Neurosci Ther. 2012 Feb;18(2):167-74.
8. Sittironnarit G, Ames D, Bush AI, et al. Effects of anticholinergic drugs on cognitive function in older Australians: results from the AIBL study. Dement Geriatr Cogn Disord. 2011;31(3):173-8.
9. Gray SL, Anderson ML, Dublin S, et al. Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study. JAMA Intern Med. 2015 Mar;175(3):401-7.
10. Salahudeen MS, Hilmer S, Nishtala PS. Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people. J Am Geriatr Soc. 2015 Jan;63(1):85-90.
11. Coupland CAC, Hill T, Dening T, et al. Anticholinergic Drug Exposure and the Risk of Dementia: A Nested Case-Control Study. JAMA Intern Med. 2019 Aug 1;179(8):1084-1093.
12. Richardson K, Fox C, Maidment I, et al. Anticholinergic drugs and risk of dementia: case-control study. BMJ. 2018 Apr 25;361:k1315.
13. Chatterjee S, Bali V, Carnahan RM, et al. Anticholinergic Medication Use and Risk of Fracture in Elderly Adults with Depression. J Am Geriatr Soc. 2016 Jul;64(7):1492-7 [abstract].
14. Sarbacker GB, Espino DV, Wood RC, et al. Total anticholinergic burden and survival within a cohort of elderly Mexican Americans. Geriatr Gerontol Int. 2017 Oct;17(10):1515-1521 [abstract].
15. Kose E, Hirai T, Seki T. Anticholinergic drugs use and risk of hip fracture in geriatric patients. Geriatr Gerontol Int. 2018 Sep;18(9):1340-1344 [abstract].
16. Kose E, Hirai T, Seki T. Assessment of aspiration pneumonia using the Anticholinergic Risk Scale. Geriatr Gerontol Int. 2018 Aug;18(8):1230-1235 [abstract].
17. Kose E, Hirai T, Seki T, et al. Anticholinergic load negatively correlates with recovery of cognitive activities of daily living for geriatric patients after stroke in the convalescent stage. J Clin Pharm Ther. 2018 Dec;43(6):799-806 [abstract].

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