

August 2017 ~ Resource #330810

Drugs With Anticholinergic Activity

Use of drugs with anticholinergic activity can increase the risk of adverse effects (e.g., delirium, cognitive impairment, dry mouth, constipation, hospitalization, falls) in the elderly.^{1,10} Anticholinergics also interact with other drugs to reduce their effectiveness (e.g., cholinesterase inhibitors like donepezil [*Aricept*], etc) or increase the risk of adverse effects (e.g., increased GI irritation with oral potassium tabs or caps).² The effects of multiple anticholinergics can add up.¹ However, it is not known whether using multiple drugs with low anticholinergic activity is as detrimental as using one or more drugs that have higher anticholinergic activity. Therefore, from a practical standpoint, it may be best to target drugs with the most anticholinergic activity when attempting to reduce anticholinergic burden. If a drug cannot be eliminated, use the lowest effective dose.⁹ Drugs with low anticholinergic activity may be good alternatives to drugs with more anticholinergic activity. For example, SSRIs with lower anticholinergic activity such as sertraline are preferred over tricyclics for treatment of depression in the elderly.⁶ Not all anticholinergics have the same clinical effects due to different affinities for the various muscarinic receptor subtypes (which have different tissue distributions) and differences in ability to cross the blood-brain barrier.⁷ The chart below groups drugs by degree of anticholinergic activity. Drugs in the “MEDIUM/HIGH Activity” column are considered a “2” or “3” on at least one of the anticholinergic scales covered at the end of the chart. Drugs listed as having strong anticholinergic properties in the Beers Criteria are also listed in this column. Drugs in the “LOW Activity” column are not more than a “1” on any of these scales. 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*.

Drugs with Potential Anticholinergic Activity		
Drug Class	MEDIUM/HIGH Activity ^{1,3,4,5,8}	LOW Activity ^{1,3,4,8}
Analgesics	Meperidine Tramadol (<i>Ultram</i>)	Celecoxib Codeine Fentanyl Morphine Oxycodone
Antibiotics	None	Ampicillin Cefoxitin Clindamycin Cycloserine (<i>Seromycin</i>)-U.S. only Gentamicin Piperacillin Vancomycin
Anticonvulsants	Carbamazepine (<i>Tegretol</i>) Oxcarbazepine (<i>Trileptal</i>)	Valproic Acid

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Drugs with Potential Anticholinergic Activity		
Drug Class	MEDIUM/HIGH Activity^{1,3,4,5,8}	LOW Activity^{1,3,4,8}
Antidepressants	Amitriptyline Amoxapine-U.S. only Clomipramine (<i>Anafranil</i>) Desipramine (<i>Norpramin</i> -U.S.) Doxepin >6 mg Imipramine (<i>Tofranil</i> -U.S.) Nortriptyline (<i>Pamelor</i> -U.S., <i>Aventyl</i> -Canada) Paroxetine (<i>Paxil</i>) Protriptyline-U.S. only Trimipramine (<i>Surmontil</i> -U.S.)	Bupropion (<i>Wellbutrin</i> , etc) Citalopram Escitalopram Fluoxetine Fluvoxamine (<i>Luvox</i>) Mirtazapine (<i>Remeron</i>) Sertraline Trazodone Venlafaxine (<i>Effexor</i>)
Antihistamines	Brompheniramine Carbinoxamine-U.S. only Cetirizine (controversial) Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Diphenhydramine Doxylamine Fexofenadine (controversial) Hydroxyzine Pyrilamine Triprolidine	Desloratadine Levocetirizine Loratadine
Antimuscarinics (Overactive Bladder Agents)	Darifenacin (<i>Enablex</i>) Fesoterodine (<i>Toviaz</i>) Flavoxate Oxybutynin (<i>Ditropan</i>) Solifenacin (<i>Vesicare</i>) Tolterodine (<i>Detrol</i>) Trospium	None The extent of anticholinergic side effects seen with these agents 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, <i>Medications for Overactive Bladder</i> , for a comparison of these drugs (U.S. subscribers; Canadian subscribers).

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Drugs with Potential Anticholinergic Activity		
Drug Class	MEDIUM/HIGH Activity^{1,3,4,5,8}	LOW Activity^{1,3,4,8}
Anti-Parkinson Agents	Amantadine Benztropine (<i>Cogentin</i>) Trihexyphenidyl	Bromocriptine Carbidopa/Levodopa Entacapone (<i>Comtan</i>) Pramipexole (<i>Mirapex</i>) Phenelzine (<i>Nardil</i>) Selegiline (<i>Eldepryl</i>)
Antipsychotics	Clomipramine (<i>Anafranil</i>) Chlorpromazine Clozapine (<i>Clozaril</i>) Fluphenazine Haloperidol Loxapine Methotrimeprazine (Canada) Olanzapine (<i>Zyprexa</i>) Perphenazine Pimozide (<i>Orap</i>) Quetiapine (<i>Seroquel</i>) Thioridazine-U.S. only Thiothixene (<i>Navane</i>) Trifluoperazine	Aripiprazole Asenapine (<i>Saphris</i>) Iloperidone Paliperidone Risperidone (<i>Risperdal</i>) Ziprasidone (<i>Geodon</i> -U.S., <i>Zeldox</i> -Canada)
Benzodiazepines	None	Alprazolam (<i>Xanax</i>) Chlordiazepoxide Clonazepam (<i>Klonopin</i> -U.S., <i>Clonapam</i> -Canada) Clorazepate Diazepam (<i>Valium</i>) Estazolam-U.S. only Flurazepam Lorazepam Midazolam Oxazepam Temazepam (<i>Restoril</i>) Triazolam

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

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Drugs with Potential Anticholinergic Activity		
Drug Class	MEDIUM/HIGH Activity ^{1,3,4,5,8}	LOW Activity ^{1,3,4,8}
Muscle Relaxants	Baclofen Carisoprodol (<i>Soma</i>)-U.S. only Cyclobenzaprine Methocarbamol (<i>Robaxin</i>) Orphenadrine Tizanidine	Pancuronium
Respiratory Meds	Pseudoephedrine Theophylline	Fluticasone/Salmeterol (<i>Advair</i>)
Other	None	Colchicine (<i>Colcrys</i> -U.S.) Ketotifen Ophthalmic Lithium Metformin Methotrexate Naratriptan Sumatriptan Zolmitriptan

This chart may not include all drugs with anticholinergic activity. A number of lists have been created to express the degree of anticholinergic activity of different drugs. The **Anticholinergic Cognitive Burden Scale** 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 clinical risk of anticholinergic effects.¹ 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 There do not appear to be studies correlating the Anticholinergic Drug Scale to bad outcomes. The **Beers Criteria** used a composite of several scales to draft a list of drugs with strong anticholinergic properties.⁵ There is a 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, and 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

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