ANTICHOLINERGICS: Reference List of Drugs with Potential Anticholinergic Effects[1, 2, 3, 4, 5]

J Bareham MSc BSP © www.RxFiles.ca July 2023

WHENEVER POSSIBLE, AVOID DRUGS WITH MODERATE TO HIGH ANTICHOLINERGIC ACTIVITY IN OLDER ADULTS (>65 YEARS OF AGE)

Beers Criteria: use of >1 med with anticholinergic properties ↑ risk of cognitive decline, delirium, & falls/fractures[5]

Low Anticholinergic Activity; Moderate/High Anticholinergic Activity; Unconfirmed Anticholinergic Activity

Antibiotics

- ampicillin
- cefoxitin ✗ ⊗
- clindamycin
- gentamicin (Oint & Sol'n NIHB covered)
- piperacillin ✗ ⊗
- vancomycin ☎ ▼

Antidepressants

TCA

amitriptyline	ELAVIL
clomipramine	ANAFRANIL
desipramine	NORPRAMIN
doxepin >6mg	SINEQUAN
imipramine	TOFRANIL
nortriptyline ☆	AVENTYL

-less anticholinergic effects than amitriptyline & imipramine

trimipramine	SURMONTIL

SSRI

citalopram ☆	CELEXA
escitalopram ☆	CIPRALEX
fluoxetine	PROZAC
fluvoxaMINE	LUVOX
paroxetine	PAXIL
sertraline ☆	ZOLOFT

Other

bupropion ☆	WELLBUTRIN, ZYBAN
desvenlafaxine	PRISTIQ ✗ ⊗
duloxetine	CYMBALTA
mirtazapine ☆	REMERON
moclobemide ☆	MANERIX
phenelzine	NARDIL
trazodone ☆	TRAZOREL
venlafaxine ☆	EFFEXOR

In older adults, citalopram & sertraline are the usually preferred SSRIs.

Antihistamines/Antipruritics

brompheniramine	COUGH & COLD PRODUCTS OTC ✗
chlorpheniramine	CHLOR-TRIPOLON OTC ✗
cyproheptadine	PERIACTIN OTC ✗ ⊗
diphenhydramine	BENADRYL OTC ✗
doxylamine	UNISOM ✗ ⊗
hydroxyzine	ATARAX
pyrilamine	MIDOL, PAMPRIN OTC ✗ ⊗
trimeprazine ◇	PANECTYL ⊗
triprolidine	COTRIDIN ✗ ⊗

Preferred Agents: cetirizine REACTINE ✗ ▼ & fexofenadine ALLEGRA ✗ ▼ (controversial rating as medium/high activity), desloratadine AERIUS ✗ ▼, loratadine CLARITIN ✗ ▼. **All available OTC.**

Antimuscarinics/Incontinence Meds

darifenacin	ENABLEX ☎ ✆
fesoterodine	TOVIAZ ☎ ✆
flavoxate	URISPAS ✗ ⊗
mirabegron ◇	MYRBETRIQ ☎ ✆
oxybutynin	DITROPAN ✗ ⊗ on XL only
propiverine	MICTORYL PEDIATRIC ☎ ▼
solifenacin	VESICARE on SPDP ▼
tolterodine l-tartrate	DETROL LA on SPDP ▼
trospium	TROSEC ☎ ✆

Antiparkinsonian

amantadine	SYMMETREL
benztropine mesylate	COGENTIN
bromocriptine	PARLODEL
carbidopa/levodopa ☆	SINEMET
entacapone	COMTAN
ethopropazine	PARSITAN
phenelzine	NARDIL
pramipexole	MIRAPEX
procyclidine	KEMADRIN
selegiline	ELDEPRYL ☎ ▼
trihexyphenidyl	ARTANE

Antipsychotics

aripiprazole ☆	ABILIFY ☎ ▼ & MAINTENA ☎ ▼
asenapine	SAPHRIS (☎-BPAD) ✆
chlorpromazine	LARGACTIL
clozapine	CLOZARIL ☎ ▼
flupentixol	FLUANXOL
fluphenazine	MODITEN
haloperidol	HALDOL
loxapine	LOXAPAC
lurasidone ◇	LATUDA ☎ ✆
methotrimeprazine	NOZINAN
olanzapine	ZYPREXA
paliperidone	INVEGA ☎ ▼ on injection only
pericyazine	NEULEPTIL
perphenazine	TRILAFON
pimozide	ORAP
quetiapine	SEROQUEL
risperidone ☆	RISPERDAL ☎ ▼ on injection only
trifluoperazine	STELAZINE
ziprasidone ☆	ZELDOX
zuclopenthixol ◇	CLOPIXOL

Antiseizure Drugs

carbamazepine	TEGRETOL
divalproex ☆	EPIVAL
oxcarbazepine	TRILEPTAL ☎ ▼
valproic acid ☆	DEPAKENE

Preferred Agents: **divalproex, gabapentin, lamotrigine, levetiracetam**

Antispasmotics

dicyclomine	FORMULEX, BENTYLOL ⊗
glycopyrrolate	ROBINUL ✗ ⊗
hyoscine butylbromide	BUSCOPAN

Benzodiazepines

alprazolam	XANAX *short-acting*
chlordiazepoxide	LIBRIUM *long-acting* ⊗
clonazepam	RIVOTRIL *intermediate-acting*
clorazepate	TRANXENE *long-acting* ⊗
diazepam	VALIUM *long-acting*
flurazepam	DALMANE *long-acting* ⊗
lorazepam ☆	ATIVAN *intermediate-acting*
midazolam	VERSED *short-acting* ✗ ⊗
oxazepam ☆	SERAX *intermediate-acting*
temazepam ☆	RESTORIL *intermediate-acting*
triazolam	HALCION *short-acting*

Avoid long- & ultra-short acting agents in older adults. (Clonazepam ok, if long-acting required e.g. chronic anxiety)

Cardiovascular Agents

atenolol	TENORMIN
captopril	CAPOTEN
chlorthalidone	GENERIC ONLY
digoxin	LANOXIN, TOLOXIN
diltiazem ☆	CARDIZEM, TIAZAC
dipyridamole	PERSANTINE, AGGRENOX ☎ ▼
disopyramide	RYTHMODAN
furosemide	LASIX
hydralazine	APRESOLINE
isosorbide	ISORDIL
metoprolol ☆	LOPRESOR
nifedipine	ADALAT
quinidine	GENERIC ONLY ✗ ⊗
triamterene	DYRENIUM
warfarin ☆	COUMADIN

Gastrointestinal Agents

atropine	LOMOTIL on SPDP ⊗
belladonna	GENERIC ONLY ✗ ⊗
bisacodyl	BISACODYL ✗ ▼ OTC
chlordiazepoxide/clidinium	LIBRAX ✗ ⊗
cimetidine	TAGAMET
dicyclomine	BENTYLOL ⊗
dimenhydrinate	GRAVOL OTC
diphenoxylate/atropine	LOMOTIL on SPDP ⊗
domperidone	MOTILIUM
famotidine ☆	PEPCID OTC & Rx
loperamide	IMODIUM OTC ☑ if used short term
meclizine	BONAMINE
metoclopramide	MAXERAN
nizatidine	AXID
prochlorperazine	STEMETIL ☑ if used short term
promethazine	PHENERGAN OTC ✗ ⊗
ranitidine	ZANTAC OTC & Rx

-low anticholinergic activity if adjusted for renal function

scopolamine	TRANSDERM V OTC on SPDP ⊗

Preferred Agents: **bisacodyl ✗, PPIs, domperidone; ondansetron; famotidine, or ranitidine if ≤150mg/day**

Respiratory Meds

aclidinium bromide	TUDORZA GENUAIR ☎ ▼
aclidinium/formoterol	DUAKLIR GENUAIR ☎ ▼
fluticasone/salmeterol	ADVAIR ☎ ✆
ipratropium/salbutamol	ATROVENT/COMBIVENT
glycopyrronium	SEEBRI BREEZHALER ☎ ▼
glycopyrronium/Indacaterol	ULTIBRO BREEZHALER ☎ ▼
pseudoephedrine	COUGH & COLD PRODUCTS OTC ✗ ⊗
theophylline	THEOLAIR, UNIPHYL
tiotropium	SPIRIVA
tiotropium/olodaterol	INSPIOLTO ☎ ▼
umeclidinium	INCRUSE ELLIPTA ☎ ▼
umeclidinium/vilanterol	ANORO ELLIPTA ☎ ▼
umeclidinium/vilanterol/fluticasone	TRELEGY ELLIPTA ☎ ✆

To minimize systemic effects of inhalational meds: avoid overuse, use aerochamber for ipratropium inhaler.

Immunosuppressants

azathioprine	IMURAN
cyclosporine	NEORAL ☎
hydrocortisone	CORTEF
methylprednisolone	MEDROL
prednisone	WINPRED

Muscle Relaxants

baclofen ☆	LIORESAL ☎ on intrathecal only
cyclobenzaprine	FLEXERIL ☎ ▼
methocarbamol	ROBAXIN OTC ✗ ⊗
orphenadrine	NORFLEX OTC ✗ ⊗
tizanidine	ZANAFLEX ☎ ✆

Opioids

meperidine	DEMEROL ✗ ⊗
codeine	☎ on controlled release only, ✆ inj & liquid
fentanyl	DURAGESIC ☎ ✆
hydromorphone ☆	DILAUDID, HYDROMORPH CONTIN ✆ on CR only
morphine ☆	STATEX, M.O.S., KADIAN ✆
oxycodone	SUPEDOL, OXY IR, OXYNEO ☎ ⊗
tramadol	ULTRAM, RALIVIA, TRIDURAL, ZYTRAM XL ✗ ⊗

Preferred Agents:

acetaminophen ✗, NSAIDs (e.g. ibuprofen, naproxen)

Miscellaneous

buspirone ◇	BUSPAR
celecoxib	CELEBREX
colchicine	GENERIC ONLY
ketotifen ophthalmic	ZADITOR ✗ ▼
lithium	CARBOLITH, DURALITH
metformin	GLUCOPHAGE, GLYCON, g
methotrexate	GENERIC ONLY
naratriptan	AMERGE ☎ ▼
pancuronium	GENERIC ONLY ✗ ⊗
sumatriptan	IMITREX ☎ ▼
zolmitriptan	ZOMIG ☎ ▼

☆ = Denotes medications with anticholinergic activity that may be better tolerated than others in that class. Whenever possible, anticholinergic medications should be avoided, and the preferred agents used.

◇ = Unable to confirm anticholinergic activity (**black** font)

AChEI = Acetylcholinesterase Inhibitor (e.g. donepezil ARICEPT, galantamine REMINYL, rivastigmine EXELON) ☎ ✆

CR = Controlled-release formulation

PPI = Proton pump inhibitor (e.g. rabeprazole)

OTC = Over-the-counter

SPDP = Saskatchewan Prescription Drug Plan

Saskatchewan Health finds co-administration of this agent **with an AChEI acceptable**

If patient is currently on this medication, Saskatchewan Health will **NOT cover an AChEI**

Anticholinergic Effects[6,7,8,9]

Dementia & Anticholinergic Medications

Diseases associated with an essential cholinergic deficit include Alzheimer's dementia, Lewy body dementia & to some extent other dementias (not frontal). Anticholinergic drugs worsen the deficit and are therefore highly problematic. **Donepezil** ARICEPT, **rivastigmine** EXELON, and **galantamine** REMINYL are reversible inhibitors of the enzyme acetylcholinesterase. Because of the mechanism of action, medications with anticholinergic effects can interfere with the activity of donepezil, rivastigmine and galantamine. The first page of this document contains a list of medications with anticholinergic effects, with an emphasis on those with moderate to high activity. Drug coverage (in Sask.) may be affected if a patient is using a medication on this list concurrently with donepezil, rivastigmine or galantamine. In addition to the concerns related to anticholinergic medications in individuals who already have a dementia diagnosis, **there is evidence that exposure to strong anticholinergic medications (esp. antidepressants, antiparkinson meds, antipsychotics, bladder antimuscarinics, & antiepileptics) is associated with an increased risk of dementia** (~10% over 1 to 11 years esp. for individuals <80 years;[10] increased dementia incidence [OR 1.17 (95%CI 1.10-1.24)] in individuals who had a anticholinergic medication 15-20 years before a dementia diagnosis;[11] 1.2x increased risk of all-cause dementia – dose-dependent relationship.[12])

Adverse Effects (AEs) of Anticholinergic Medications

The use of medications with anticholinergic activity comes with the risk of AEs in older adults (e.g., cognitive dysfunction/decline, delirium, sedation, orthostatic hypotension, falls, fractures, urinary retention). Avoiding the use of medications with anticholinergic properties in older adults is the ideal, however minimizing their use may also be a strategy for minimizing the risk of AEs. Also, selecting medications with low anticholinergic activity is preferred over those with higher anticholinergic activity. However, individuals who take multiple medications with low anticholinergic activity may also have an increased risk of AEs. Even small increases in the anticholinergic burden increases the risk of morbidity, and a higher anticholinergic burden increases the risk of cardiovascular disease and mortality in older individuals.[13,14,15]

Spectrum of Anticholinergic Side-Effects

Mild	Moderate	Severe
• Dryness of mouth (modest)	• Moderately disturbing dry mouth/thirst • Speech problems • Reduced appetite	• Difficulty chewing, swallowing, speaking • Impaired perception of taste & texture of food • Dental decay/caries, periodontal disease, denture misfit • Mucosal damage – ulceration of gums & buccal mucosa • Malnutrition • Respiratory infection
• Mild dilatation of pupils	• Inability to accommodate • Vision disturbances • Dizziness	• Increased risk of accidents & falls leading to ↓ function • Exacerbation/precipitation of acute angle closure glaucoma • Photophobia
• Mild constipation	• Esophagitis • Reduced gastric secretions, gastric emptying (atony) • Reduced peristalsis, constipation	• Fecal impaction (in patients with constipation) • Altered absorption of concomitant medications • Paralytic ileus, pseudo-obstruction
• Urinary hesitancy		• Urinary retention, urinary tract infection (in patients with urinary hesitancy)
• Mild/transient increased HR	• Increased heart rate	• Conduction disturbances supraventricular tachyarrhythmias • Exacerbation of angina • Congestive heart failure • Myocardial infarction
• Decreased sweating		• Thermoregulatory impairment leading to hyperthermia (heat stroke). {Additional risk if also on diuretic.}
• Drowsiness • Fatigue • Mild amnesia • Inability to concentrate	• Excitement • Restlessness • Confusion • Memory impairment	• Profound restlessness & disorientation, agitation • Hallucinations, delirium • Ataxia, muscle twitching, hyperreflexia, seizures • Exacerbation of cognitive impairment (in patients with dementia)

Tips to Deal with Anticholinergic Side-Effects

General approach:

- Identify the cause
- Discontinue unnecessary offending medications
- Reduce the dose
- Look for effective alternatives that are less likely to cause the side effect

Dry Mouth:

- 80% of the most commonly prescribed medications can cause dry mouth (e.g. incontinence meds, Parkinson's meds, antidepressants, antipsychotics, NSAIDs, opioids, muscle relaxants, antihistamines, benzodiazepines, antihypertensives [clonidine, alpha-blockers, beta-blockers, calcium channel blockers, diuretics, ACE inhibitors]).
- When appropriate, instruct patients to take meds associated with dry mouth early in the day since salivary production is lowest at night.
- Divided doses may also be less likely to cause dry mouth than a single large dose.
- Consider therapeutic alternatives that are less likely to cause dry mouth.
- Avoid: alcohol-containing mouthwashes, alcoholic beverages, caffeine, tobacco.
- Swish mouth with water every 2 hours.
- Drink plenty of fluids while eating to make swallowing easier; avoid foods that are hard to chew.
- Chewing sugar-free gum or sucking on sugar-free candy mechanically stimulates salivation and can be recommended to promote salivation in patients with functioning salivary glands.
- Nondrug options: bedroom humidifier; artificial saliva or oral lubricants (**MOUTH KOTE**, **BIOTENE GEL**, **ORAL BALANCE GEL**, **MOI-STIR SPRAY** ▼ for Palliative care).
- Pharmacologic options: pilocarpine (muscarinic agonist) 5 to 10mg of pilocarpine 3 or 4 times daily to a max of 30mg daily – will cause salivation in patients with functioning salivary glands. Duration of action is 3 to 5 hours. Common side effects (dose-dependent): sweating, nausea, rhinitis, flushing, urinary frequency. **CI**: uncontrolled asthma, narrow-angle glaucoma, acute iritis. **Pilocarpine eye drops** cost significantly less than pilocarpine tablets and can be used orally for treatment of dry mouth. **4 drops of the 2% solution, directly on tongue or add to small amount of water & swish and swallow, 3 times daily** (can swish and spit to reduce systemic side effects).

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