PHARMACIST'S LETTER

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PRESCRIBER'S LETTER

Potentially Harmful Drugs in the Elderly: Beers List

In 1991, Dr. Mark Beers and colleagues published a methods paper describing the development of a consensus list of medicines considered to be inappropriate for long-term care facility residents.[12] The American Geriatrics Society Beers Criteria or "Beers list" is now in its fifth permutation.[1] It is intended for use by clinicians in outpatient as well as inpatient settings (**but not hospice or palliative care**) to improve the care of patients 65 years of age and older.[1] It includes medications that should be avoided, and medications that should be used with extra caution, either in all elderly or in certain populations.[1] New to the 2015 version is a list of potentially harmful drug-drug interactions in seniors, as well as a list of medications that may need to be avoided or their dosage reduced based on renal function.[1] This information is not comprehensive; medications and interactions were chosen for inclusion based on their potential to cause harm.[1] Also new this year is a list of alternatives to medications on the "avoid" list or on the potentially harmful drug-disease interactions list.[5] An additional tool for improving care in the elderly is the START and STOPP criteria. Neither has been convincingly shown to reduce morbidity, mortality, or cost but are often used by organizations as quality measures. Use the list to identify red flags that might require intervention or close monitoring, not the final word on medication appropriateness. Medication use decisions must be individualized.[14] If the decision is made to stop a potentially inappropriate medication, tapering may be needed (e.g., benzodiazepines, corticosteroids, acetylcholinesterase inhibitors, PPIs).[14] The chart below summarizes the 2015 Beers list, potential therapeutic alternatives, and other considerations.

A = avoid in most elderly (**does not apply to palliative care/hospice patients**)
C = use with caution in elderly
H = High-risk meds in the elderly per CMS Quality Measure (CMS156v1) and Star Ratings Measure (D11). Designated CMS high-risk meds based on previous (i.e., 2012) Beers list. Update forthcoming. (Note: CMS high-risk med trimethobenzamide is no longer included on the 2015 Beers list.)

--Information in table is from reference 1, unless otherwise specified.--

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Analgesics (also see NSAIDs, below)		
Meperidine (**A**, **H**) (also see Opioids)	Neurotoxicity, delirium, cognitive impairment, poor efficacy (orally)	Of special concern in patients with chronic kidney disease, delirium, or risk of delirium. Avoid combining with two or more other CNS-active drugs (fall risk). Alternative opioids: oxycodone/acetaminophen, morphine, or tramadol.[5] Alternatives for neuropathic pain may include SNRIs, gabapentin, pregabalin, capsaicin, or lidocaine patch (U.S.), depending on concomitant conditions. For more help choosing, see our *PL Chart*, *Pharmacotherapy of Neuropathic Pain*.

More. . .

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
Opioids in patient with a history of falls or fractures	Unsteady gait, psychomotor impairment, syncope	Acceptable for recent fracture or joint replacement. Consider reducing other concomitant medication(s) that can cause falls. Employ fall-prevention strategies. Avoid combining with two or more other CNS-active drugs (fall risk). For alternatives for different types of pain, see our *PL Charts*, *Pharmacotherapy of Neuropathic Pain*, *Analgesics for Osteoarthritis*, *Treatment of Acute Low Back Pain*, *Treatment of Chronic Low Back Pain*, *Analgesics for Acute Pain*.
Pentazocine (**A**, **H**) (also see Opioids)	More CNS effects (e.g., confusion, hallucinations) than other opioids Mixed agonist/antagonist	Avoid combining with two or more other CNS-active drugs (fall risk). Alternative opioids: oxycodone/acetaminophen, morphine, or tramadol.[5] Alternatives for neuropathic pain may include SNRIs, gabapentin, pregabalin, capsaicin, or lidocaine patch (U.S.), depending on concomitant conditions. For more help choosing, see our *PL Chart*, *Pharmacotherapy of Neuropathic Pain*.
Tramadol (*Ultram*, etc) in patient with seizures or CrCl <30 mL/min.	Lowers seizure threshold. May be acceptable if seizures are well controlled and alternative cannot be used. Renal impairment: increased risk of CNS adverse effects. Avoid extended-release product. Reduce dose of immediate-release product.	Avoid combining with two or more other CNS-active drugs (fall risk). For alternatives for different types of pain, see our *PL Charts*, *Pharmacotherapy of Neuropathic Pain*, *Analgesics for Osteoarthritis*, *Treatment of Acute Low Back Pain*, *Treatment of Chronic Low Back Pain*, *Analgesics for Acute Pain*.

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Anticonvulsants		
Anticonvulsants in patient with history of fall or fracture, except for seizure or mood disorder (also see individual agents for additional, agent-specific concerns)	Unsteady gait, psychomotor impairment, syncope	For new-onset seizures, "newer" agents preferred (e.g., lamotrigine, levetiracetam).[5] Also see our *PL Chart*, *Comparison of Antiepileptic Drugs* Consider bone protection (e.g., bisphosphonate).[5] Alternatives for neuropathic pain may include SNRIs, gabapentin, pregabalin, capsaicin, or lidocaine patch (U.S.), depending on concomitant conditions. For more help choosing, see our *PL Chart*, *Pharmacotherapy of Neuropathic Pain*.
Carbamazepine (**C**) (also see Anticonvulsants)	SIADH. Check sodium when starting or changing dose.	For alternative anticonvulsants, see our *PL Chart*, *Comparison of Antiepileptic Drugs*.
Gabapentin in patient with CrCl <60 mL/min. (also see Anticonvulsants)	Increased risk of central nervous system adverse effects. Reduce dose.	For alternative anticonvulsants, see our *PL Chart*, *Comparison of Antiepileptic Drugs*. Alternatives for neuropathic pain may include SNRIs, pregabalin, capsaicin, or lidocaine patch (U.S.), depending on concomitant conditions. For more help choosing, see our *PL Chart*, *Pharmacotherapy of Neuropathic Pain*.
Levetiracetam in patient with CrCl 80 mL/min or less	Increased risk of central nervous system adverse effects. Reduce dose.	For alternative anticonvulsants, see our *PL Chart*, *Comparison of Antiepileptic Drugs*.
Oxcarbazepine (**C**) (also see Anticonvulsants)	SIADH. Check sodium when starting or changing dose.	For alternative anticonvulsants, see our *PL Chart*, *Comparison of Antiepileptic Drugs*. Alternatives for neuropathic pain may include SNRIs, gabapentin, pregabalin, capsaicin, or lidocaine patch (U.S.), depending on concomitant conditions. For more help choosing, see our *PL Chart*, *Pharmacotherapy of Neuropathic Pain*.

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Pregabalin in patient with CrCl <60 mL/min. (also see Anticonvulsants)	Increased risk of central nervous system adverse effects. Reduce dose.	For alternative anticonvulsants, see our *PL Chart*, *Comparison of Antiepileptic Drugs*. Alternatives for neuropathic pain may include SNRIs, gabapentin, capsaicin, or lidocaine patch (U.S.), depending on concomitant conditions. For more help choosing, see our *PL Chart*, *Pharmacotherapy of Neuropathic Pain*.
Antidepressants		
Bupropion in patient with seizures	Lowers seizure threshold. May be acceptable if seizures are well controlled and alternative cannot be used.	For help choosing an alternate antidepressant, see our *PL Chart*, *Choosing and Switching Antidepressants*.
Duloxetine in patient with CrCl <30 mL/min.	Increased risk of nausea or diarrhea. Avoid.	
Maprotiline in patient with seizures	Lowers seizure threshold. May be acceptable if seizures are well controlled and alternative cannot be used.	
Mirtazapine (*Remeron*) (**C**)	SIADH. Check sodium when starting or changing dose.	
Paroxetine (**A**) (also see SSRIs)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention), sedation, orthostatic hypotension	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Avoid combining with two or more other CNS-active drugs (fall risk). For help choosing an alternate antidepressant, see our *PL Chart*, *Choosing and Switching Antidepressants*.
SNRI (**C**) (also see Duloxetine)	SIADH. Check sodium when starting or changing dose.	

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
SSRIs in patient with history of falls or fractures (also see Paroxetine)	Unsteady gait, psychomotor impairment, syncope	Consider reducing other concomitant medication(s) that can cause falls. Employ fall-prevention strategies. Avoid combining with two or more other CNS-active drugs (fall risk). Alternatives for depression: SNRIs (not duloxetine if CrCl <30 mL/min.), bupropion (not in patients with seizures).[1,5] For help choosing, see our *PL Chart*, *Choosing and Switching Antidepressants*.
SSRIs (**C**) (also see Paroxetine)	SIADH. Check sodium when starting or changing dose.	Avoid combining with two or more other CNS-active drugs (fall risk).
Tricyclic antidepressants: amitriptyline (**A**, **H**), amoxapine (**A**), clomipramine (**A**, **H**), desipramine (**A**), doxepin (>6 mg/day [**A, H**]), imipramine (**A**, **H**), nortriptyline (**A**), protriptyline (**A**), trimipramine (**A**, **H**)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Sedation Orthostatic hypotension, unsteady gait, psychomotor impairment SIADH. Check sodium when starting or changing dose.	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, history of falls or fractures, lower urinary symptoms, or BPH (avoid in men). Tertiary amines (amitriptyline, clomipramine, doxepin, imipramine, trimipramine) of special concern in patients with syncope due to risk of orthostatic hypotension. Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Avoid combining with two or more other CNS-active drugs (fall risk). Alternatives for depression: SSRI (not paroxetine; not for patient with fall/fracture risk), SNRI (not duloxetine if CrCl <30 mL/min.), bupropion (not in patient with seizures).[1,5] Alternatives for neuropathic pain may include SNRIs, gabapentin, pregabalin, capsaicin, or lidocaine patch (U.S.), depending on concomitant conditions. For more help choosing, see our *PL Chart*, *Pharmacotherapy of Neuropathic Pain*. Alternatives for insomnia: Consider nonpharmacologic interventions.[5] To help explain these to patients, use our *PL Patient Education Handout*, *Strategies for a Good Night's Sleep*. Pharmacologic alternatives include low-dose trazodone, low-dose doxepin, or ramelteon (U.S.).[13]

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Antigout		
Colchicine in patient with CrCl <30 mL/min.	Increased risk of bone marrow toxicity, GI adverse effects, neuromuscular adverse effects. Use reduced dose. Monitor for adverse effects.	Alternatives: corticosteroid.[17]
Probenecid in patient with CrCl <30 mL/min.	Ineffective. Avoid.	Alternative uricosuric agents (if xanthine oxidase inhibitor not appropriate): fenofibrate, losartan, sulfinpyrazone (Canada).[17]
Antihistamines		
Anticholinergic antihistamines (**A**, **H**): brompheniramine, carbinoxamine, chlorpheniramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, diphenhydramine (oral), doxylamine, hydroxyzine, triprolidine (see CNS section for **meclizine**)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Sedating Elimination reduced in elderly Tolerance to hypnotic effect	Diphenhydramine may be appropriate in acute treatment of severe allergic reactions. Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternatives: for allergy, nasal saline, nasal steroid, 2nd generation antihistamine (e.g., cetirizine, fexofenadine, loratadine).[5] For sleep, consider nonpharmacologic interventions. To help explain these to patients, use our *PL Patient Education Handout*, *Strategies for a Good Night's Sleep*. Pharmacologic alternatives possibly include low-dose trazodone, low-dose doxepin, or ramelteon (U.S.).[13]
Antihypertensives		
Alpha-blockers (doxazosin [*Cardura*], prazosin [*Minipress*], terazosin [*Hytrin*]) (**A**)	Orthostatic hypotension	Of special concern in patients with syncope, and women with urinary incontinence (especially when combined with a loop diuretic). Alternatives for hypertension: thiazide, ACEI, ARB, long-acting CCB.[5] For help choosing, see our *PL Algorithm*, *Stepwise Treatment of Hypertension* (U.S. subscribers; Canadian subscribers).

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
Amiloride in patient with CrCl<30 mL/min. or taking ACEI.	Renal impairment: increased potassium and decreased sodium. Avoid. Do not combine with ACEI except in patients with hypokalemia on ACEI.	Alternatives for hypertension: thiazide, ACEI, ARB, long-acting CCB.[5] For help choosing, see our *PL Algorithm*, *Stepwise Treatment of Hypertension* (U.S. subscribers; Canadian subscribers).
Clonidine (*Catapres*), as first-line antihypertensive (**A**)	Orthostatic hypotension, bradycardia, CNS adverse effects	
Diuretics (C)	SIADH or hyponatremia. Check sodium when starting or changing dose.	
Guanfacine (**A**, **H**)	Orthostatic hypotension, bradycardia, CNS adverse effects	
Methyldopa (**A**, **H**)		
Nifedipine, short-acting (**A**, **H**)	Hypotension, myocardial ischemia	Alternative dihydropyridine CCBs: amlodipine, felodipine, nifedipine extended-release.[5]
Reserpine >0.1 mg/d (**A**, **H**)	Orthostatic hypotension, bradycardia, CNS adverse effects	Alternatives for hypertension: thiazide, ACEI, ARB, long-acting CCB.[5] For help choosing, see our *PL Algorithm*, *Stepwise Treatment of Hypertension* (U.S. subscribers; Canadian subscribers).
Triamterene in patient with CrCl <30 mL/min. or taking ACEI	Renal impairment: increased potassium and decreased sodium. Avoid. Do not combine with ACEI except in patients with hypokalemia on ACEI.	
Vasodilators in patient with history of syncope (**C**)	More frequent episodes of syncope	

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Antiplatelet Agents and Anticoagulants		
Apixaban (*Eliquis*) in patient with CrCl <25 mL/min.	Bleeding risk. Avoid.	Consider warfarin.[6]
Aspirin for primary prevention in patients age 80 years and up (**C**), or at doses >325 mg/d (**A**)	Lack of evidence of benefit for primary prevention in patients 80 years and older May cause or worsen ulcers.	Doses >325 mg/d of special concern in patients with a history of ulcers.
Dabigatran (*Pradaxa*) in patients ≥75 years of age, and in patients with CrCl <30 mL/min (**C**)	Higher bleeding risk in patients 75 years of age and older. Use caution. Lack of efficacy/safety evidence in CrCl <30 mL/min., and increased bleeding risk. Avoid.	Consider warfarin.[6]
Dipyridamole, oral short-acting (**A**, **H**)	More effective options available, orthostatic hypotension	Alternatives for secondary stroke prevention: See our *PL Chart*, *Antiplatelets for Recurrent Ischemic Stroke*.
Edoxaban (U.S.; *Savaysa*) in patients with CrCl <50 mL/min., or >95 mL/min.	Renal impairment: bleeding risk increased. Reduce dose if CrCl 30 to 50 mL/min. Avoid if CrCl <30 mL/min. CrCl >95 mL/min.: potential for reduced efficacy in A Fib.[4] Avoid.[1]	Consider warfarin.[6]
Enoxaparin in patients with CrCl <30 mL/min.	Bleeding risk. Reduce dose.	Alternative: unfractionated heparin[15]
Fondaparinux in patients with CrCl <30 mL/min.	Bleeding risk. Avoid.	Alternatives: unfractionated heparin (preferred for "treatment" doses) or enoxaparin.[15]

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
Prasugrel (*Effient*) in patients 75 years of age and older (**C**)	Bleeding risk	Benefit may balance bleeding risk in patients with high cardiac risk (e.g., diabetes, history of heart attack).
Rivaroxaban (*Xarelto*) in patient with CrCl <50 mL/min.	Bleeding risk. Reduce dose if CrCl 30 to 50 mL/min. Avoid if CrCl <30 mL/min.	Consider warfarin.[6] Also use with caution in the elderly.[2,3]
Ticlopidine (*Ticlid*) (**A**, **H**)	Safer alternatives available	For help choosing an alternative, see our *PL Chart*, *Comparison of Oral Antiplatelets*.
Antipsychotics		
Antipsychotics (**A**) (any; also see individual agents for additional, agent-specific concerns)	Risk of stroke and death in dementia patients May cause or worsen delirium or cognitive impairment. Unsteady gait, psychomotor impairment, syncope may lead to falls. Dopamine-receptor blockade may worsen Parkinson's disease. SIADH. Check sodium when starting or changing dose.	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, history of falls or fractures, or Parkinson's disease (except aripiprazole, clozapine, or quetiapine) (also see individual agents) Nonanticholinergic agent acceptable for bipolar disorder, schizophrenia, antiemetic during chemo, or dementia- or delirium-related behavioral problems if nondrug therapy has failed or can't be used, and the patient may harm self or others.[1,5] Use lowest dose for shortest time possible.[5] Avoid combining with two or more other CNS-active drugs (fall risk).
Chlorpromazine in patient with syncope, seizures, BPH (also see Antipsychotics)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Risk of orthostatic hypotension Lowers seizure threshold.	In seizure patients, may be acceptable if seizures are well controlled and alternative cannot be used. Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
Clozapine in patient with seizures or BPH (also see Antipsychotics)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Lowers seizure threshold.	May be acceptable if seizures are well controlled and alternative cannot be used. Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Loxapine in patient with BPH (also see Antipsychotics)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention)	Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Olanzapine in patient with syncope, seizures, or BPH (also see Antipsychotics)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Risk of orthostatic hypotension Lowers seizure threshold.	In seizure patients, may be acceptable if seizures are well controlled and alternative cannot be used. Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Perphenazine in patient with BPH (also see Antipsychotics)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention)	Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Thioridazine (**H**) in patient with syncope, seizures, or BPH (also see Antipsychotics)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Risk of orthostatic hypotension Lowers seizure threshold	In seizure patients, may be acceptable if seizures are well controlled and alternative cannot be used. Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).

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Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Thiothixene in patient with seizures (also see Antipsychotics)	Lowers seizure threshold	May be acceptable if seizures are well controlled and alternative cannot be used.
Trifluoperazine in patient with BPH (also see Antipsychotics)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention)	Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Anxiolytics		
Benzodiazepines (**A**)	Increased sensitivity and impaired metabolism (long-acting agents) increases risk of cognitive impairment, unsteady gait, psychomotor impairment, accidents, and delirium.	Long-acting agents may be acceptable for seizures, REM sleep disorders, benzodiazepine or alcohol withdrawal, severe generalized anxiety disorder, and periprocedural use. Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, or history of falls or fractures. Avoid combining with two or more other CNS-active drugs (fall risk). Alternatives for anxiety: buspirone, SSRI (not paroxetine; not in patients with fall/fracture risk), SNRI For sleep, consider nonpharmacologic interventions.[5] To help explain these to patients, use our *PL Patient Education Handout*, *Strategies for a Good Night's Sleep*. Pharmacologic alternatives include low-dose trazodone, low-dose doxepin, or ramelteon (U.S.).[13]
Meprobamate (**A**, **H**)	Sedation, dependence	Alternatives for anxiety: buspirone, SSRI (not paroxetine; not for patients with fall/fracture risk), SNRI.[1,5]
Cardiac Drugs		
Amiodarone first-line for atrial fibrillation (unless patient has heart failure or left ventricular hypertrophy, and rhythm control is desired) (**A**)	More toxic than other treatments for atrial fibrillation.	For help choosing an alternative for A Fib, see our *PL Chart*, *2014 AHA/ACC A Fib Guidelines: Focus on Pharmacotherapy*. Amiodarone increases warfarin bleeding risk. If warfarin and amiodarone must be used together, monitor INR.

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
Calcium channel blockers, nondihydropyridine (diltiazem, verapamil) in heart failure with reduced ejection fraction	May worsen heart failure	For help choosing an alternate antihypertensive, see our *PL Algorithm*, *Stepwise Treatment of Hypertension* (U.S. subscribers; Canadian subscribers).
Cilostazol (U.S.) in heart failure	May cause fluid retention	For help choosing an alternative, see our *PL Chart*, *Comparison of Oral Antiplatelets*.
Digoxin first-line for A Fib or heart failure (**A**), or in doses >0.125 mg/day. (**A**)(**H**)	May increase mortality in A Fib and heart failure. Unclear benefit on hospitalization in heart failure, and may increase mortality Reduced renal clearance increases risk of toxicity.	For help choosing an alternate for A Fib, see our *PL Chart*, *2014 AHA/ACC A Fib Guidelines: Focus on Pharmacotherapy*. For help choosing an alternate for heart failure, see our *PL Chart*, *Heart Failure Treatment at a Glance*.
Disopyramide (**A, H**)	Negative inotrope; may cause heart failure Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention)	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternatives for A Fib: beta-blocker, diltiazem, verapamil (rate control); dofetilide, flecainide, propafenone (rhythm control).[5] For help choosing, see our *PL Chart*, *2014 AHA/ACC A Fib Guidelines: Focus on Pharmacotherapy*.
Dronedarone in patient with permanent atrial fibrillation or severe or recently decompensated heart failure (**A**)	Worse outcome in these patients	For help choosing an alternative, see our *PL Chart*, *2014 AHA/ACC A Fib Guidelines: Focus on Pharmacotherapy*

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
Spironolactone CrCl <30 mL/min.	Hyperkalemia. Avoid.	For help choosing an alternate antihypertensive, see our *PL Algorithm*, *Stepwise Treatment of Hypertension* (U.S. subscribers; Canadian subscribers). For help choosing an alternate for heart failure, see our *PL Chart*, *Heart Failure Treatment at a Glance*.
Central Nervous System Agents, misc.		
Acetylcholinesterase inhibitors (e.g., donepezil, etc), in patient with syncope	Orthostatic hypotension or bradycardia	Alternative: memantine[7]
Dimenhydrinate (**A**)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention), sedation. Elimination reduced in elderly.	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternatives for Meniere's disease: Sodium restriction, diuretics[8]
Lithium in patient taking ACEI or loop diuretic	Risk of lithium toxicity.	Avoid combination, but if used, monitor lithium levels. For alternatives for bipolar disorder, see our *PL Detail-Document*, *Pharmacotherapy of Bipolar Disorder in Adults*.
Meclizine (**A**)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention), sedation. Elimination reduced in elderly.	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternatives for Meniere's disease: Sodium restriction, diuretics[8]
Chemotherapy		
Carboplatin (**C**)	SIADH. Check sodium when starting or changing dose.	
Cisplatin (**C**)		
Cyclophosphamide (**C**)		
Vincristine (**C**)		

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Diabetes Drugs		
Chlorpropamide (**A**, **H**)	Long duration of action, prolonged hypoglycemia; SIADH	Alternative sulfonylurea: glipizide, gliclazide (Canada)[5]
Glyburide (**A**, **H**)	Long duration of action, prolonged hypoglycemia	Alternative sulfonylurea: glipizide, gliclazide (Canada)[5]
Insulin, sliding scale (i.e., sole use of as-needed short- or rapid-acting insulin with no basal or scheduled insulin) (**A**)	Hypoglycemia; poor efficacy	See our *PL Algorithm*, *Initiation and Adjustment of Insulin Regimens for Type 2 Diabetes* (U.S. subscribers; Canadian subscribers), for help dosing and titrating insulin.
Pioglitazone in heart failure	Fluid retention may worsen heart failure	For alternatives, see our *PL Chart*, *Drugs for Type 2 Diabetes* (U.S. subscribers) or *Stepwise Treatment of Type 2 Diabetes* (Canadian subscribers).
Rosiglitazone in heart failure	Fluid retention may worsen heart failure	For alternatives, see our *PL Chart*, *Drugs for Type 2 Diabetes* (U.S. subscribers) or *Stepwise Treatment of Type 2 Diabetes* (Canadian subscribers).
Gastrointestinal Drugs		
Antispasmodics: belladonna alkaloids, clidinium (in *Librax*), dicyclomine (*Bentyl* [U.S.], *Bentylol* [Canada]), hyoscyamine (*Levsin* [U.S.]), propantheline (U.S.), scopolamine (**A**)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Unclear efficacy	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). For alternatives for irritable bowel, see our *PL Chart*, *Treatments for Irritable Bowel Syndrome*.

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Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
H2-blocker in patient with dementia, cognitive impairment, delirium or high risk of delirium, taking theophylline (cimetidine), or CrCl <50 mL/min.	Has central nervous system effects that can cause or worsen these conditions Cimetidine increases theophylline levels. Renal impairment: increased risk of mental status changes.	Avoid cimetidine in patient taking theophylline. Reduce dose if CrCl <50 mL/min. Alternative: proton pump inhibitor (see Proton Pump Inhibitor listing for caveats).[5]
Metoclopramide, except for gastroparesis (**A**)	Extrapyramidal side effects, tardive dyskinesia	Of special concern in patients with Parkinson's disease, due to dopamine receptor blockade. Alternatives for nausea: serotonin antagonists (e.g., ondansetron, etc).[10]
Mineral oil, oral (**A**)	Aspiration	For alternatives, see our *PL Algorithm*, *Treatment of Constipation in Adults*.
Prochlorperazine in patient with dementia, cognitive impairment, Parkinson's disease, delirium or high risk of delirium, lower urinary tract symptoms, or BPH	Anticholinergic action may cause confusion, cognitive impairment, delirium, or urinary retention. Dopamine-receptor blockade may worsen Parkinson's disease.	Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternatives for nausea: serotonin antagonists (e.g., ondansetron, etc).[10]
Promethazine in patient with dementia, cognitive impairment, Parkinson's disease, delirium or high risk of delirium, lower urinary tract symptoms, or BPH (**H**)	Anticholinergic action may cause confusion, cognitive impairment, delirium, or urinary retention. Dopamine-receptor blockade may worsen Parkinson's disease.	Avoid in men. Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternatives for nausea: serotonin antagonists (e.g., ondansetron, etc).[10]
Proton pump inhibitors, scheduled use for >8 weeks (**A**)	Risk of *C. difficile* pseudomembranous colitis, bone loss, fractures	Scheduled use for >8 weeks acceptable for patients with high ulcer risk (e.g., taking corticosteroids or chronic NSAID), erosive esophagitis, hypersecretory disorder, Barrett's esophagus, confirmed need for maintenance (e.g., failed "drug holiday;" H2-blocker failure).

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Hormones		
Corticosteroids (oral, parenteral) in patient with delirium or high risk of delirium	May cause or worsen delirium	Use lowest effective dose for shortest time necessary. Avoid combining with NSAIDs (GI ulcer/bleed risk). Alternatives depend on indication.
Estrogen (oral, transdermal), with or without progestin (**A**, **H**)	Breast cancer, endometrial cancer, worsening of incontinence; not cardioprotective; lacks cognitive protection	Alternatives: low-dose vaginal estrogens acceptable for vaginal symptoms and prevention of lower urinary tract infections.[1] For vasomotor symptoms, SSRI (not paroxetine), SNRI, gabapentin.[5] For help choosing, see our *PL Detail-Document*, *Nonhormonal Therapy for Hot Flashes*.
Growth hormone, except after pituitary removal (**A**)	Edema, arthralgia, carpal tunnel syndrome, gynecomastia, insulin resistance; little effect on muscle mass	Consider high-calorie supplements to promote weight gain.[9]
Megestrol (**A**, **H**)	Thrombosis, death; minimal effect on weight	Consider high-calorie supplements to promote weight gain.[9]
Testosterone, methyltestosterone, except for confirmed symptomatic hypogonadism (U.S.) (**A**)	Prostate cancer, cardiac events	See our *PL Detail-Document*, *The Use of Testosterone and the Aging Male*, for more information about the risks and appropriate use of testosterone.
Thyroid, desiccated (**A**, **H**)	Cardiac adverse effects	Alternative: levothyroxine
Hypnotics		
Antihistamines (see listing above)		
Barbiturates (any) (**A**, **H**)	Dependence, tolerance, risk of overdose (narrow therapeutic window)	Of special concern in patients with delirium or high risk of delirium. Alternatives for seizures: see our *PL Chart*, *Comparison of Antiepileptic Drugs*. For sleep, consider nonpharmacologic interventions.[5]

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Benzodiazepines (see listing under Anxiolytics)		
Nonbenzodiazepine, benzodiazepine receptor agonists ("Z drugs;" eszopiclone, zopiclone[a] [Canada], zolpidem, zaleplon [U.S.]) (**A** [for any duration], **H**)	Increased sensitivity increases risk of cognitive impairment, unsteady gait, psychomotor impairment, accidents, and delirium. Unfavorable risk/benefit ratio for insomnia	Of special concern in patient with dementia, cognitive impairment, delirium or high risk of delirium, or history of falls or fractures. Avoid combining with two or more other CNS-active drugs (fall risk). Consider nonpharmacologic interventions.[5] To help explain these to patients, use our *PL Patient Education Handout*, *Strategies for a Good Night's Sleep*. Pharmacologic alternatives include low-dose trazodone, low-dose doxepin, or ramelteon (U.S.).[13]
Musculoskeletal Agents		
Benztropine (**A**, **H**) (oral; U.S.)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Not recommended to prevent antipsychotic-associated extrapyramidal effects; not very effective for Parkinson's disease	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, history of falls or fractures, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternative for Parkinson's disease: levodopa/carbidopa[5]
Muscle relaxants (**A**, **H**): carisoprodol (U.S.; *Soma*), chlorzoxazone, cyclobenzaprine, metaxalone (U.S.; *Skelaxin*), methocarbamol (e.g., *Robaxin*), orphenadrine	Anticholinergic effects (cyclobenzaprine, orphenadrine; e.g., confusion, dry mouth, constipation, urinary retention), sedation, fracture Questionable efficacy at doses tolerated in elderly	Cyclobenzaprine and orphenadrine of particular concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternatives: acetaminophen, nonacetylated salicylate, NSAID (ibuprofen or naproxen if no heart or renal failure, with gastroprotection if used for >7 days)[5]

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Trihexyphenidyl (**A**, **H**)	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation, urinary retention) Not recommended to prevent antipsychotic-associated extrapyramidal effects; not very effective for Parkinson's disease	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, history of falls or fractures, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline). Alternative for Parkinson's disease: levodopa/carbidopa.[5]
NSAIDs		
Aspirin >325 mg/day (**A**)	Ulcer/GI bleed/perforation risk	GI risk factors: age >75 years of age, corticosteroids, anticoagulants, antiplatelets. Protect with proton pump inhibitor or misoprostol if chronic use (>7 days) unavoidable.[1,5] Avoid combining with oral or parenteral corticosteroids, or warfarin.
NSAIDs, chronic use (**A**), indomethacin (any use)(**A**, **H**), ketorolac (any use)(**A**, **H**)	Ulcer/GI bleed/perforation risk (particularly ketorolac), central nervous system effects (indomethacin), acute kidney injury (ketorolac), worsening heart failure, worsening renal function in chronic kidney disease (CrCl <30 mL/min)	Of special concern in patients with ulcer history. GI risk factors: age >75 years of age, corticosteroids, anticoagulants, antiplatelets. Protect with proton pump inhibitor or misoprostol if chronic use (>7 days) unavoidable.[1,5] Avoid combining with oral or parenteral corticosteroids, or warfarin. Alternatives: acetaminophen, nonacetylated salicylate, capsaicin, lidocaine patch (U.S.), topical NSAID, SNRI.[5] If no heart or renal failure and use unavoidable, choose ibuprofen or naproxen, with gastroprotection if used >7 days.[5]

Drug or Drug Class	**Concern(s)**	**Other Considerations (e.g., drug interactions, alternatives)**[b]
COX-2 inhibitors in heart failure or CrCl <30 mL/min.	Worsening heart failure. Worsening renal function in chronic kidney disease (CrCl <30 mL/min)	Alternatives: acetaminophen, SNRI (not duloxetine), topical capsaicin, lidocaine patch (U.S.)[5]
Respiratory Drugs		
Atropine (**A**)	Anticholinergic effects (i.e., may cause confusion, cognitive impairment, delirium, dry mouth, constipation, or urinary retention)	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Homatropine (**A**)	Anticholinergic effects (i.e., may cause confusion, cognitive impairment, delirium, dry mouth, constipation, or urinary retention)	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium, lower urinary symptoms, or BPH (avoid in men). Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Phenylephrine (oral) in patient with insomnia	Central nervous system stimulation	Alternatives: for allergy, nasal saline, nasal corticosteroid, 2nd generation antihistamine, nasal decongestant (for ≤5 days); for colds, nasal saline, nasal decongestant (for ≤5 days), humidifier, raising head of bed[16]
Pseudoephedrine in patients with insomnia		
Theophylline in patient with insomnia		Alternatives: see our *PL Toolboxes*, *Improving COPD Care* and *Improving Asthma Care*.
Stimulant Drugs		
Amphetamines in patient with insomnia	Central nervous system stimulation	
Armodafinil in patient with insomnia		
Methylphenidate in patient with insomnia		
Modafinil in patient with insomnia		

Drug or Drug Class	Concern(s)	Other Considerations (e.g., drug interactions, alternatives)[b]
Urinary Drugs		
Desmopressin	Hyponatremia	Alternatives: address underlying cause of nocturia (e.g., hyperglycemia, urinary infection, medication [calcium channel blocker, beta-blocker, cholinesterase inhibitors], etc). Consider 5-alpha reductase inhibitor for BPH.[11]
Nitrofurantoin in patients with CrCl <30 mL/min (**A**), or for chronic use (**A**, **H**)	Pulmonary toxicity, peripheral neuropathy, hepatotoxicity, especially with chronic use. Safety and efficacy (i.e., inadequate urine concentration) concerns in patients with CrCl <30 mL/min.	New cohort data suggest nitrofurantoin can be effective and have minimal risk in moderate renal impairment.[18]
Urinary antimuscarinics (e.g., darifenacin, fesoterodine, flavoxate, oxybutynin, solifenacin, tolterodine, trospium) in patient with dementia, cognitive impairment, chronic constipation, delirium, or high risk of delirium	Anticholinergic effects (e.g., confusion, cognitive impairment, delirium, dry mouth, constipation)	Of special concern in patients with dementia, cognitive impairment, delirium or high risk of delirium. Avoid combining drugs with anticholinergic effects (risk of cognitive decline).
Vasodilators (CNS)		
Ergoloid mesylates (**A**, **H**) Isoxsuprine (**H**)(U.S. only)	Lack of efficacy	Alternatives: Acetylcholinesterase inhibitors (not in patients with syncope), memantine[5]

Abbreviations: ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BPH = benign prostatic hyperplasia; CCB = calcium channel blocker; CrCl = creatinine clearance; CNS = central nervous system; COX-2 = cyclo-oxygenase-2; NSAID = nonsteroidal anti-inflammatory drug; SIADH = syndrome of inappropriate antidiuretic hormone secretion; SNRI = selective norepinephrine serotonin reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

a. Zopiclone (Canada; *Imovane*, etc) not included in Beers, but prudent to consider same precautions as for eszopiclone.
b. Alternatives may not be appropriate for all patients.

Users of this PL Detail-Document 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.

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