Table 5. 2019 American Geriatrics Society Beers Criteria® for Potentially Clinically Important Drug-Drug Interactions That Should Be Avoided in Older Adults

Object Drug and Class	Interacting Drug and Class	Risk Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
RAS inhibitor (ACEIs, ARBs, aliskiren) or potassium-sparing diuretics (amiloride, triamterene)	Another RAS inhibitor (ACEIs, ARBs, aliskiren)	Increased risk of hyperkalemia	Avoid routine use in those with chronic kidney disease stage 3a or higher	Moderate	Strong
Opioids	Benzodiazepines	Increased risk of overdose	Avoid	Moderate	Strong
Opioids	Gabapentin, pregabalin	Increased risk of severe sedation-related adverse events, including respiratory depression and death	Avoid; exceptions are when transitioning from opioid therapy to gabapentin or pregabalin, or when using gabapentinoids to reduce opioid dose, although caution should be used in all circumstances.	Moderate	Strong
Anticholinergic	Anticholinergic	Increased risk of cognitive decline	Avoid; minimize number of anticholinergic drugs (Table 7)	Moderate	Strong
Antidepressants (TCAs, SSRIs, and SNRIs) Antipsychotics Antiepileptics Benzodiazepines and nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (ie, "Z-drugs") Opioids	Any combination of three or more of these CNS-active drugs[a]	Increased risk of falls (all) and of fracture (benzodiazepines and nonbenzodiazepine, benzodiazepine receptor agonist hypnotics)	Avoid total of three or more CNS-active drugs[a]; minimize number of CNS-active drugs	Combinations including benzodiazepines and nonbenzodiazepine, benzodiazepine receptor agonist hypnotics *or* opioids: high All other combinations: moderate	Strong
Corticosteroids, oral or parenteral	NSAIDs	Increased risk of peptic ulcer disease or gastrointestinal bleeding	Avoid; if not possible, provide gastrointestinal protection	Moderate	Strong
Lithium	ACEIs	Increased risk of lithium toxicity	Avoid; monitor lithium concentrations	Moderate	Strong
Lithium	Loop diuretics	Increased risk of lithium toxicity	Avoid; monitor lithium concentrations	Moderate	Strong
Peripheral α-1 blockers	Loop diuretics	Increased risk of urinary incontinence in older women	Avoid in older women, unless conditions warrant both drugs	Moderate	Strong
Phenytoin	Trimethoprim-sulfamethoxazole	Increased risk of phenytoin toxicity	Avoid	Moderate	Strong
Theophylline	Cimetidine	Increased risk of theophylline toxicity	Avoid	Moderate	Strong
Theophylline	Ciprofloxacin	Increased risk of theophylline toxicity	Avoid	Moderate	Strong
Warfarin	Amiodarone	Increased risk of bleeding	Avoid when possible; if used together, monitor INR closely	Moderate	Strong
Warfarin	Ciprofloxacin	Increased risk of bleeding	Avoid when possible; if used together, monitor INR closely	Moderate	Strong
Warfarin		Increased risk of bleeding		Moderate	Strong

(Continued)

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Table 5 (Contd.)

Object Drug and Class	Interacting Drug and Class	Risk Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
	Macrolides (excluding azithromycin)		Avoid when possible; if used together, monitor INR closely		
Warfarin	Trimethoprim-sulfamethoxazole	Increased risk of bleeding	Avoid when possible; if used together, monitor INR closely	Moderate	Strong
Warfarin	NSAIDs	Increased risk of bleeding	Avoid when possible; if used together, monitor closely for bleeding	High	Strong

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CNS, central nervous system; INR, international normalized ratio; NSAID, nonsteroidal anti-inflammatory drug; RAS, renin-angiotensin system; SNRI, serotonin- norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

[a]CNS-active drugs: antiepileptics; antipsychotics; benzodiazepines; nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; TCAs; SSRIs; SNRIs; and opioids.

The 2019 update has a similar number of changes to the 2015 update but fewer changes than the 2012 update. This is likely because, with the support of the AGS and the expert panel, the criteria have been regularly updated about every 3 years since 2012. In 2019, 25 medications or medication classes to be avoided outright or in a disease condition were dropped from the AGS Beers Criteria® (Table 8). A few were also moved to a new table category or modified (Table 10). For medications to be removed from the AGS Beers Criteria®, the panel had to have new evidence or a strong rationale, for reasons such as the literature showed a change in evidence that cast new doubt on their "avoid" status. Finally, some drugs or drug-disease combinations were omitted because they are not disproportionately relevant to the older adult population; this included the criteria on drugs to avoid in adults with chronic seizures or epilepsy and in adults with insomnia.

Four new medications or medication classes were added to the list of drugs to be used with caution (Table 4; additions are also summarized in Table 9). Dextromethorphan/quinidine was added because of its limited efficacy, concerns for clinically significant drug interactions, and potentially increased risk of falls in older adults. TMP-SMX was placed in the "use with caution table" because of increased risk of hyperkalemia when used concurrently with an ACEI or ARB in the presence of decreased creatinine clearance.[13,14] Rivaroxaban was also added to the use with caution table for adults 75 years or older. Other important changes in the use with caution table included lowering the age threshold in the aspirin for primary prevention recommendation from 80 years or younger to 70 years or younger on the basis of emerging evidence of a major increase in the risk of bleeding at a lower age.[15] The Aspirin in Reducing Events in the Elderly (ASPREE) trial, which was published outside the window of our literature search, found that low-dose aspirin used for primary prevention in older adults did not confer a reduction in mortality, disability-free survival, or cardiovascular events.[16,17] In a few instances, the level of evidence was revised based on new literature and the improved modified grading method. For instance, H2-receptor antagonists were removed from the list of drugs to avoid in dementia, and the evidence level for H2-receptor antagonists was decreased to low (from moderate in 2015) for drugs to avoid in delirium.[18] Again in 2019, the panel clarified the language for sliding-scale insulin because this continued to be an area of confusion for clinicians.

Importantly, several drugs were added to the drug-disease and drug-drug interactions tables (Tables 3 and 5). Notably, SNRIs were added to the list of antidepressant drug classes to avoid in persons with a history of falls or fractures.[19,20] For this criterion, the level of evidence for opioids was changed to "moderate"; all other drugs remain at high. Two new drug-drug interactions involving opioids were added, reflecting evidence of substantial harms that can occur when opioids are used concurrently with benzodiazepines or gabapentinoids. Though these drug interactions involving opioids are problematic in all persons, they are growing increasingly common and may lead to greater harm in vulnerable older adults. These concerns need to be balanced with the need to treat chronic pain. A recent review of deaths from opioids concluded that the burden of opioid overdose in older adults requires special attention, noting the largest

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