

# American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

*The American Geriatrics Society 2012 Beers Criteria Update Expert Panel*

Potentially inappropriate medications (PIMs) continue to be prescribed and used as first-line treatment for the most vulnerable of older adults, despite evidence of poor outcomes from the use of PIMs in older adults. PIMs now form an integral part of policy and practice and are incorporated into several quality measures. The specific aim of this project was to update the previous Beers Criteria using a comprehensive, systematic review and grading of the evidence on drug-related problems and adverse drug events (ADEs) in older adults. This was accomplished through the support of The American Geriatrics Society (AGS) and the work of an interdisciplinary panel of 11 experts in geriatric care and pharmacotherapy who applied a modified Delphi method to the systematic review and grading to reach consensus on the updated 2012 AGS Beers Criteria. Fifty-three medications or medication classes encompass the final updated Criteria, which are divided into three categories: potentially inappropriate medications and classes to avoid in older adults, potentially inappropriate medications and classes to avoid in older adults with certain diseases and syndromes that the drugs listed can exacerbate, and finally medications to be used with caution in older adults. This update has much strength, including the use of an evidence-based approach using the Institute of Medicine standards and the development of a partnership to regularly update the Criteria. Thoughtful application of the Criteria will allow for (a) closer monitoring of drug use, (b) application of real-time e-prescribing and interventions to decrease ADEs in older adults, and (c) better patient outcomes. *J Am Geriatr Soc* 2012.

**Key words:** Beers list; medications; Beers Criteria; drugs; older adults

**M**edication-related problems are common, costly, and often preventable in older adults and lead to poor out-

comes. Estimates from past studies in ambulatory and long-term care settings found that 27% of adverse drug events (ADEs) in primary care and 42% of ADEs in long-term care were preventable, with most problems occurring at the ordering and monitoring stages of care.<sup>1,2</sup> In a study of the 2000/2001 Medical Expenditure Panel Survey, the total estimated healthcare expenditures related to the use of potentially inappropriate medications (PIMs) was \$7.2 billion.<sup>3</sup>

Avoiding the use of inappropriate and high-risk drugs is an important, simple, and effective strategy in reducing medication-related problems and ADEs in older adults. Methods to address medication-related problems include implicit and explicit criteria. Explicit criteria can identify high-risk drugs using a list of PIMs that have been identified through expert panel review as having an unfavorable balance of risks and benefits by themselves and considering alternative treatments available. A list of PIMs was developed and published by Beers and colleagues for nursing home residents in 1991 and subsequently expanded and revised in 1997 and 2003 to include all settings of geriatric care.<sup>4-6</sup> Implicit criteria may include factors such as therapeutic duplication and drug-drug interactions. PIMs determined by explicit criteria (Beers Criteria) have also recently been found to identify other aspects of inappropriate medication use identified by implicit criteria.<sup>7</sup>

As summarized in two reviews, a number of investigators in rigorously designed observational studies have shown a strong link between the medications listed in the Beers Criteria and poor patient outcomes (e.g., ADEs, hospitalization, mortality).<sup>7-14</sup> Moreover, research has shown that a number of PIMs have limited effectiveness in older adults and are associated with serious problems such as delirium, gastrointestinal bleeding, falls, and fracture.<sup>8,12</sup> In addition to identifying drugs for which safer pharmacological alternatives are available, in many instances a safer nonpharmacological therapy could be substituted for the use of these medications, highlighting that a “less-is-more approach” is often the best way to improve health outcomes in older adults.<sup>15</sup>

Since the early 1990s, the prevalence of PIM usage has been examined in more than 500 studies, including a number of long-term care, outpatient, acute care, and community settings. Despite this preponderance of information, many PIMs continue to be prescribed and used as first-

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line treatment for the most vulnerable of older adults.<sup>16,17</sup> These studies illustrate that more work is needed to address the use of PIMs in older adults, and there remains an important role in policy, research, and practice for an explicit list of medications to avoid in older adults. Because an increasing number of interventions have been successful in decreasing the use of these drugs and improving clinical outcomes,<sup>18,19</sup> PIMs now form an integral part of policy and practice in the Centers for Medicare and Medicaid Services (CMS) regulations and are used in Medicare Part D. They are also used as a quality measure in the National Committee for Quality Assurance (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS). Several stakeholders, including CMS, NCQA, and the Pharmacy Quality Alliance (PQA) have identified the Beers Criteria as an important quality measure. In addition, a few studies have begun to identify nonpharmacological alternatives to inappropriate medications<sup>20</sup> and are incorporating Beers Criteria PIMs into electronic health records as an aid to real-time e-prescribing.<sup>19</sup>

An update of the Beers Criteria should include a clear approach to reviewing and grading the evidence for the drugs to avoid. In addition, the criteria need to be regularly updated as new drugs come to the market, as new evidence emerges related to the use of these medications, and as new methods to assess the evidence develop. Being able to update these criteria quickly and transparently is crucial to their continued use as decision-making tools, because regular updates will improve their relevancy, dissemination, and usefulness in clinical practice.

The 2012 update of the Beers Criteria heralds a new partnership with the American Geriatrics Society (AGS). This partnership allows for regular, transparent, systematic updates and support for the wider input and dissemination of the criteria by expert clinicians for their use in research, policy, and practice. To keep this tool relevant, the updated 2012 AGS Beers Criteria must be current with other methods for determining best-practice guidelines. A rigorous systematic review was performed to update and expand the criteria. As in the past, this update will categorize PIMs into two broad groups: medications to avoid in older adults regardless of diseases or conditions and medications considered potentially inappropriate when used in older adults with certain diseases or syndromes. A third group, medications that should be used with caution, has been added. Medications in this group were initially considered for inclusion as PIMs. In these cases, the consensus view of the panel (described below) was that there were a sufficient number of plausible reasons why use of the drug in certain individuals would be appropriate but that the potential for misuse or harm is substantial and thus merits an extra level of caution in prescribing. In some cases, these medications were new to the market, and evidence was still emerging.

## OBJECTIVES

The specific aim is to:

Update the previous Beers Criteria using a comprehensive, systematic review and grading of the evidence on drug-related problems and ADEs in older adults.

The strategies to achieve this aim are to:

1. Incorporate new evidence on currently listed PIMs and evidence from new medications or conditions not addressed in the previous (2003) update.
2. Grade the strength and quality of each PIM statement based on level of evidence and strength of recommended grading.
3. Convene an interdisciplinary panel of 11 experts in geriatric care and pharmacotherapy who will apply a modified Delphi method to the systematic review and grading to reach consensus on the updated 2012 AGS Beers Criteria.
4. Incorporate needed exceptions into the criteria as deemed clinically appropriate by the panel. These evidence-based exceptions will be designed to make the criteria more individualized to clinical care and more relevant across settings of care.

## INTENT OF CRITERIA

The 2012 AGS Beers Criteria are intended for use in all ambulatory and institutional settings of care for populations aged 65 and older in the United States. The primary target audience is the practicing clinician. Researchers, pharmacy benefit managers, regulators, and policy-makers also use the criteria widely. The intentions of the criteria include improving the selection of prescription drugs by clinicians and patients, evaluating patterns of drug use within populations, educating clinicians and patients on proper drug usage, and evaluating health-outcome, quality of care, cost, and utilization data.

The goal of the 2012 AGS Beers Criteria is to improve care of older adults by reducing their exposure to PIMs. This is accomplished by their use as an educational tool and a quality measure—two uses that are not always in agreement. These criteria are not meant to be applied in a punitive manner. Prescribing decisions are not always clear cut, and clinicians must consider multiple factors. Quality measures must be clearly defined, easily applied, and measured with limited information. The panel considered both roles during deliberations. The panel's review of evidence at times identified subgroups of individuals who should be exempt from the criteria or for whom only a specific criterion applies. Such a criterion may not be easily applied as a quality measure. These applications were balanced with the needs and complexities of the individual. The panel felt that a criterion could not be expanded to include all adults aged 65 and older when only individuals with specific characteristics may benefit or be at greater risk of harm.

## METHODS

For this new update, the AGS employed a well-tested framework that has long been used for development of clinical practice guidelines.<sup>6,21–23</sup> Specifically, the framework involved the appointment of an 11-member interdisciplinary expert panel with relevant clinical expertise and experience and an understanding of how the criteria have been previously used. To ensure that potential conflicts of interest are disclosed and addressed appropriately, panelists disclosed potential conflicts of interest with the panel at the beginning. Each panelist's potential conflict of inter-

ests are provided toward the end of this article. This framework also involved a development process that included a systematic literature review and evaluation of the evidence base by the expert panel. Finally, the Institute of Medicine's 2011 report on developing practice guidelines,<sup>23</sup> which included a period for public comments, guided the framework. These three framework principles are described in greater detail below.

### Literature Search

The literature from December 1, 2001 (the end of the previous panel's search) to March 30, 2011, was searched to identify published systematic reviews and meta-analyses that were relevant to the project. Search terms included adverse drug reactions, adverse drug events, medication problems, polypharmacy, inappropriate drug use, suboptimal drug therapy, drug monitoring, pharmacokinetics, drug interactions, and medication errors. Terms were searched alone and in combination. Search limits included human subjects, English language, and aged 65 and older. Data sources for the initial search included Medline, the Cochrane Library (Cochrane Database of Systematic Reviews), International Pharmaceutical abstracts, and references lists of selected articles that the panel co-chairs identified.

The initial search identified 25,549 citations, of which 6,505 were selected for preliminary review. The panel co-chairs reviewed 2,267 citations, of which 844 were excluded for not meeting the study purpose or not containing primary data. An additional search was conducted with the additional terms drug–drug and drug–disease interactions, pharmacoepidemiology, drug safety, geriatrics, and elderly prescribing. An additional search for randomized clinical trials and postmarketing and observational studies published between 2009 and 2011 was conducted using terms related to major drug classes and conditions, delimited by more-general topics (e.g., adverse drug reactions, Beers Criteria, suboptimal prescribing, and interventions). Previous searches were used to develop additional terms to be

included in subsequent searches, such as a list of authors whose work was relevant to the goals of the project. When evidence was sparse on older medications, searches were conducted on drug class and individual medication names and included older search dates for these drugs. The co-chairs continually reviewed the updated search results for articles that might be relevant to the project. Panelists were also asked to forward pertinent citations that might be useful for revising the previous Beers Criteria or supporting additions to them.

At the time of the panel's face-to-face meeting, the co-chairs had selected 2,169 unduplicated citations for the full panel review. This total included 446 systematic reviews or meta-analyses, 629 randomized controlled trials, and 1,094 observational studies. Additional articles were found in a manual search of the reference lists of identified articles and the panelist's files, book chapter, and recent review articles, with 258 citations selected for the final evidence tables to support the list of drugs to avoid.

### Panel Selection

After consultation with the AGS, the co-chairs identified prospective panel members with recognized expertise in geriatric medicine, nursing, pharmacy practice, research, and quality measures. Other factors that influenced selection were the desire to have interdisciplinary representation, a range of medical specialties, and representation from different practice settings (e.g., long-term care, ambulatory care, geriatric mental health, palliative care and hospice). In addition to the 11-member panel, representatives from CMS, NCQA, and PQA were invited to serve as ex-officio members.

Each expert panel member completed a disclosure form that was shared with the entire panel before the process began. Potential conflicts of interest were resolved by the panel co-chairs and were available during the open comment period. Panel members who disclosed affiliations or financial interests with commercial entities are listed under the disclosures section of this article.

**Table 1. Designations of Quality and Strength of Evidence**

| Designation                       | Description  |
|-----------------------------------|--|
| <i>Quality of evidence</i>        |  |
| High                              | Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes ( $\geq 2$ consistent, higher-quality randomized controlled trials or multiple, consistent observational studies with no significant methodological flaws showing large effects)   |
| Moderate                          | Evidence is sufficient to determine effects on health outcomes, but the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes ( $\geq 1$ higher-quality trial with $> 100$ participants; $\geq 2$ higher-quality trials with some inconsistency; $\geq 2$ consistent, lower-quality trials; or multiple, consistent observational studies with no significant methodological flaws showing at least moderate effects) limits the strength of the evidence |
| Low                               | Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality studies, important flaws in study design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes  |
| <i>Strength of recommendation</i> |  |
| Strong                            | Benefits clearly outweigh risks and burden OR risks and burden clearly outweigh benefits   |
| Weak                              | Benefits finely balanced with risks and burden   |
| Insufficient                      | Insufficient evidence to determine net benefits or risks   |

**Table 2. 2012 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults**

| Organ System or Therapeutic Category or Drug   | Rationale  | Recommendation   | Quality of Evidence   | Strength of Recommendation |
|--|--|--|---|----------------------------|
| <i>Anticholinergics (excludes TCAs)</i>  |  |  |   |                            |
| First-generation antihistamines (as single agent or as part of combination products)<br>Brompheniramine<br>Carbinoxamine<br>Chlorpheniramine<br>Clemastine<br>Cyproheptadine<br>Dexbrompheniramine<br>Dexchlorpheniramine<br>Diphenhydramine (oral)<br>Doxylamine<br>Hydroxyzine<br>Promethazine<br>Triprolidine | Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; greater risk of confusion, dry mouth, constipation, and other anticholinergic effects and toxicity. Use of diphenhydramine in special situations such as acute treatment of severe allergic reaction may be appropriate | Avoid  | Hydroxyzine and promethazine: high;<br>All others: moderate | Strong                     |
| Antiparkinson agents<br>Benztropine (oral)<br>Trihexyphenidyl  | Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more-effective agents available for treatment of Parkinson disease  | Avoid  | Moderate  | Strong                     |
| Antispasmodics<br>Belladonna alkaloids<br>Clidinium-chlordiazepoxide<br>Dicyclomine<br>Hyoscyamine<br>Propantheline<br>Scopolamine   | Highly anticholinergic, uncertain effectiveness  | Avoid except in short-term palliative care to decrease oral secretions   | Moderate  | Strong                     |
| <i>Antithrombotics</i>   |  |  |   |                            |
| Dipyridamole, oral short acting* (does not apply to extended-release combination with aspirin)   | May cause orthostatic hypotension; more-effective alternatives available; intravenous form acceptable for use in cardiac stress testing  | Avoid  | Moderate  | Strong                     |
| Ticlopidine*   | Safer effective alternatives available   | Avoid  | Moderate  | Strong                     |
| <i>Anti-infective</i>  |  |  |   |                            |
| Nitrofurantoin   | Potential for pulmonary toxicity; safer alternatives available; lack of efficacy in patients with CrCl < 60 mL/min due to inadequate drug concentration in the urine   | Avoid for long-term suppression; avoid in patients with CrCl < 60 mL/min | Moderate  | Strong                     |
| <i>Cardiovascular</i>  |  |  |   |                            |
| Alpha <sub>1</sub> blockers<br>Doxazosin<br>Prazosin<br>Terazosin  | High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile   | Avoid use as an antihypertensive   | Moderate  | Strong                     |
| Alpha agonists, central<br>Clonidine<br>Guanabenz*<br>Guanfacine*<br>Methyldopa*<br>Reserpine (> 0.1 mg/d)*  | High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension   | Avoid clonidine as a first-line antihypertensive. Avoid others as listed | Low   | Strong                     |

(Continued)

Table 2. (Contd.)

| Organ System or Therapeutic Category or Drug   | Rationale   | Recommendation  | Quality of Evidence | Strength of Recommendation |
|--|---|---|---------------------|----------------------------|
| Antiarrhythmic drugs (Class Ia, Ic, III)<br>Amiodarone<br>Dofetilide<br>Dronedarone<br>Flecainide<br>Ibutilide<br>Procainamide<br>Propafenone<br>Quinidine<br>Sotalol                      | Data suggest that rate control yields better balance of benefits and harms than rhythm control for most older adults.<br>Amiodarone is associated with multiple toxicities, including thyroid disease, pulmonary disorders, and QT- interval prolongation | Avoid antiarrhythmic drugs as first-line treatment of atrial fibrillation   | High                | Strong                     |
| Disopyramide*  | Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred   | Avoid   | Low                 | Strong                     |
| Dronedarone  | Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or heart failure. In general, rate control is preferred over rhythm control for atrial fibrillation   | Avoid in patients with permanent atrial fibrillation or heart failure   | Moderate            | Strong                     |
| Digoxin > 0.125 mg/d   | In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity; slow renal clearance may lead to risk of toxic effects  | Avoid   | Moderate            | Strong                     |
| Nifedipine, immediate release*   | Potential for hypotension; risk of precipitating myocardial ischemia  | Avoid   | High                | Strong                     |
| Spirinolactone > 25 mg/d   | In heart failure, the risk of hyperkalemia is higher in older adults especially if taking > 25 mg/d or taking concomitant NSAID, angiotensin converting-enzyme inhibitor, angiotensin receptor blocker, or potassium supplement                           | Avoid in patients with heart failure or with a CrCl < 30 mL/min   | Moderate            | Strong                     |
| <i>Central nervous system</i>  |   |   |                     |                            |
| Tertiary TCAs, alone or in combination:<br>Amitriptyline<br>Chlordiazepoxide-amitriptyline<br>Clomipramine<br>Doxepin > 6 mg/d<br>Imipramine<br>Perphenazine-amitriptyline<br>Trimipramine | Highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low-dose doxepin ( $\leq 6$ mg/d) is comparable with that of placebo   | Avoid   | High                | Strong                     |
| Antipsychotics, first (conventional) and second (atypical) generation (see Table 8 for full list)  | Increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia  | Avoid use for behavioral problems of dementia unless nonpharmacological options have failed and patient is threat to self or others | Moderate            | Strong                     |
| Thioridazine<br>Mesoridazine   | Highly anticholinergic and risk of QT-interval prolongation   | Avoid   | Moderate            | Strong                     |

(Continued)

Table 2. (Contd.)

| Organ System or Therapeutic Category or Drug   | Rationale  | Recommendation   | Quality of Evidence                       | Strength of Recommendation              |
|--|--|--|---|---|
| Barbiturates<br>Amobarbital*<br>Butobarbital*<br>Butalbital<br>Mephobarbital*<br>Pentobarbital*<br>Phenobarbital<br>Secobarbital*  | High rate of physical dependence; tolerance to sleep benefits; risk of overdose at low dosages   | Avoid  | High                                      | Strong                                  |
| Benzodiazepines<br><i>Short and intermediate acting:</i><br>Alprazolam<br>Estazolam<br>Lorazepam<br>Oxazepam<br>Temazepam<br>Triazolam<br><i>Long acting:</i><br>Clorazepate<br>Chlordiazepoxide<br>Chlordiazepoxide-amitriptyline<br>Clidinium-chlordiazepoxide<br>Clonazepam<br>Diazepam<br>Flurazepam<br>Quazepam | Older adults have increased sensitivity to benzodiazepines and slower metabolism of long-acting agents. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults<br>May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, perioperative anesthesia, end-of-life care | Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium   | High                                      | Strong                                  |
| Chloral hydrate*   | Tolerance occurs within 10 days, and risks outweigh benefits in light of overdose with doses only 3 times the recommended dose   | Avoid  | Low                                       | Strong                                  |
| Meprobamate  | High rate of physical dependence; very sedating  | Avoid  | Moderate                                  | Strong                                  |
| Nonbenzodiazepine hypnotics<br>Eszopiclone<br>Zolpidem<br>Zaleplon   | Benzodiazepine-receptor agonists that have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); minimal improvement in sleep latency and duration  | Avoid chronic use (> 90 days)  | Moderate                                  | Strong                                  |
| Ergot mesylates*<br>Isoxsuprine*   | Lack of efficacy   | Avoid  | High                                      | Strong                                  |
| <i>Endocrine</i>   |  |  |   |   |
| Androgens<br>Methyltestosterone*<br>Testosterone   | Potential for cardiac problems and contraindicated in men with prostate cancer   | Avoid unless indicated for moderate to severe hypogonadism   | Moderate                                  | Weak                                    |
| Desiccated thyroid   | Concerns about cardiac effects; safer alternatives available   | Avoid  | Low                                       | Strong                                  |
| Estrogens with or without progestins   | Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women<br>Evidence that vaginal estrogens for treatment of vaginal dryness is safe and effective in women with breast cancer, especially at dosages of estradiol < 25 µg twice weekly  | Avoid oral and topical patch.<br>Topical vaginal cream: acceptable to use low-dose intravaginal estrogen for the management of dyspareunia, lower urinary tract infections, and other vaginal symptoms | Oral and patch: high<br>Topical: moderate | Oral and patch: strong<br>Topical: weak |
| Growth hormone   | Effect on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose  | Avoid, except as hormone replacement after pituitary gland removal   | High                                      | Strong                                  |

(Continued)

Table 2. (Contd.)

| Organ System or Therapeutic Category or Drug  | Rationale  | Recommendation   | Quality of Evidence                       | Strength of Recommendation |
|---|--|--|---|----------------------------|
| Insulin, sliding scale  | Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting   | Avoid  | Moderate                                  | Strong                     |
| Megestrol   | Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults   | Avoid  | Moderate                                  | Strong                     |
| Sulfonylureas, long duration<br>Chlorpropamide<br>Glyburide   | Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes syndrome of inappropriate antidiuretic hormone secretion. Glyburide: greater risk of severe prolonged hypoglycemia in older adults   | Avoid  | High                                      | Strong                     |
| <i>Gastrointestinal</i>   |  |  |   |                            |
| Metoclopramide  | Can cause extrapyramidal effects including tardive dyskinesia; risk may be even greater in frail older adults  | Avoid, unless for gastroparesis  | Moderate                                  | Strong                     |
| Mineral oil, oral   | Potential for aspiration and adverse effects; safer alternatives available   | Avoid  | Moderate                                  | Strong                     |
| Trimethobenzamide   | One of the least effective antiemetic drugs; can cause extrapyramidal adverse effects  | Avoid  | Moderate                                  | Strong                     |
| <i>Pain</i>   |  |  |   |                            |
| Meperidine  | Not an effective oral analgesic in dosages commonly used; may cause neurotoxicity; safer alternatives available  | Avoid  | High                                      | Strong                     |
| Non-COX-selective NSAIDs, oral<br>Aspirin > 325 mg/d<br>Diclofenac<br>Diflunisal<br>Etodolac<br>Fenoprofen<br>Ibuprofen<br>Ketoprofen<br>Meclofenamate<br>Mefenamic acid<br>Meloxicam<br>Nabumetone<br>Naproxen<br>Oxaprozin<br>Piroxicam<br>Sulindac<br>Tolmetin | Increases risk of GI bleeding and peptic ulcer disease in high-risk groups, including those aged > 75 or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. Use of proton pump inhibitor or misoprostol reduces but does not eliminate risk. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months and in approximately 2–4% of patients treated for 1 year. These trends continue with longer duration of use | Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent (proton pump inhibitor or misoprostol) | Moderate                                  | Strong                     |
| Indomethacin<br>Ketorolac, includes parenteral  | Increases risk of GI bleeding and peptic ulcer disease in high-risk groups. (See above Non-COX selective NSAIDs.)<br>Of all the NSAIDs, indomethacin has most adverse effects  | Avoid  | Indomethacin: moderate<br>Ketorolac: high | Strong                     |

(Continued)

Table 2. (Contd.)

| Organ System or Therapeutic Category or Drug   | Rationale   | Recommendation | Quality of Evidence | Strength of Recommendation |
|--|---|----------------|---------------------|----------------------------|
| Pentazocine*   | Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs; is also a mixed agonist and antagonist; safer alternatives available | Avoid          | Low                 | Strong                     |
| Skeletal muscle relaxants<br>Carisoprodol<br>Chlorzoxazone<br>Cyclobenzaprine<br>Metaxalone<br>Methocarbamol<br>Orphenadrine | Most muscle relaxants are poorly tolerated by older adults because of anticholinergic adverse effects, sedation, risk of fracture; effectiveness at dosages tolerated by older adults is questionable   | Avoid          | Moderate            | Strong                     |

The primary target audience is the practicing clinician. The intentions of the criteria are to improve the selection of prescription drugs by clinicians and patients; evaluate patterns of drug use within populations; educate clinicians and patients on proper drug usage; and evaluate health-outcome, quality of care, cost, and utilization data.

\* Infrequently used drugs.

CNS = central nervous system; COX = cyclooxygenase; CrCl = creatinine clearance; GI = gastrointestinal; NSAID = nonsteroidal anti-inflammatory drug; TCA = tricyclic antidepressant.

Correction made after online publication February 29, 2012: Table 2 has been updated.

### Development Process

The co-chairs and AGS staff edited the survey used in the previous Beers Criteria development process, excluding products no longer marketed. The resulting survey had three parts: medications currently listed as potentially inappropriate for older adults independent of diseases or conditions, medications currently listed as potentially inappropriate when used in older adults with certain diseases or conditions, and new submissions from the panel. Each panelist was asked to complete the survey using a 5-point Likert scale ranging from strongly agree to strongly disagree (or no opinion). Ratings were tallied and returned to the panel along with each panelist's original ratings. Two conference calls allowed for review of survey ratings, discussion, and consensus building.

The panel convened for a 2-day in-person meeting on August 2 and 3, 2011, to review the second draft of the survey and the results of the literature search. Panel discussions were used to define terms and to address questions of consistency, the inclusion of infrequently used drugs, the best strategies for evaluating the evidence, and the consolidation or expansion of individual criterion. The panel then split into four groups, with each assigned a specific set of criteria for evaluation. Groups were assigned as closely as possible according to specific area of clinical expertise (e.g., cardiovascular, central nervous system). Groups reviewed the literature search, selected citations relevant to their assigned criteria, and determined which citations should be included in an evidence table. During this process, panelists were provided copies of abstracts and full-text articles. The groups then presented their findings to the full panel for comment and consensus. After the meeting, each group met in a conference call to resolve any questions or to include additional supporting literature.

An independent researcher prepared evidence tables, which were distributed to the four criteria-specific groups.

Each panelist independently rated the quality of evidence and strength of recommendation for each criterion using the American College of Physicians' Guideline Grading System<sup>24</sup> (Table 1), which is based on the Grades of Recommendation Assessment, Development, and Evaluation (GRADE) scheme developed previously.<sup>25</sup> AGS staff compiled the panelist ratings for each group and returned them to that group, which then reached consensus in conference call. Additional literature was obtained and included as needed. When group consensus could not be reached, the full panel reviewed the ratings and worked through any differences until they reached consensus. For some criteria, the panel provided a "strong" recommendation even though the quality of evidence was low or moderate. In such cases, the strength of recommendation was based on potential severity of harm and the availability of treatment alternatives.

### RESULTS

Fifty-three medications or medication classes encompass the final updated 2012 AGS Beers Criteria, which are divided into three categories (Tables 2–4). Tables were constructed and organized according to major therapeutic classes and organ systems.

Table 2 shows the 34 potentially inappropriate medications and classes to avoid in older adults. Notable new additions include megestrol, glyburide, and sliding-scale insulin.

Table 3 summarizes potentially inappropriate medications and classes to avoid in older adults with certain diseases and syndromes that the drugs listed can exacerbate. Notable new inclusions are thiazolidinediones or glitazones with heart failure, acetylcholinesterase inhibitors with history of syncope, and selective serotonin reuptake inhibitors with falls and fractures.



**Table 3. 2012 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug–Disease or Drug–Syndrome Interactions That May Exacerbate the Disease or Syndrome**

| Disease or Syndrome               | Drug  | Rationale   | Recommendation  | Quality of Evidence   | Strength of Recommendation   |
|-----------------------------------|---|---|---|---|--|
| <i>Cardiovascular</i>             |   |   |   |   |  |
| Heart failure                     | NSAIDs and COX-2 inhibitors<br>Nondihydropyridine CCBs (avoid only for systolic heart failure)<br>Diltiazem<br>Verapamil<br>Pioglitazone, rosiglitazone<br>Cilostazol<br>Dronedarone                        | Potential to promote fluid retention and exacerbate heart failure   | Avoid   | NSAIDs: moderate<br>CCBs: moderate<br>Thiazolidinediones (glitazones): high<br>Cilostazol: low<br>Dronedarone: moderate | Strong   |
| Syncope                           | AChEIs<br>Peripheral alpha blockers<br>Doxazosin<br>Prazosin<br>Terazosin<br>Tertiary TCAs<br>Chlorpromazine, thioridazine, and olanzapine  | Increases risk of orthostatic hypotension or bradycardia  | Avoid   | Alpha blockers: high<br>TCAs, AChEIs, and antipsychotics: moderate  | AChEIs and TCAs: strong<br>Alpha blockers and antipsychotics: weak |
| <i>Central nervous system</i>     |   |   |   |   |  |
| Chronic seizures or epilepsy      | Bupropion<br>Chlorpromazine<br>Clozapine<br>Maprotiline<br>Olanzapine<br>Thioridazine<br>Thiothixene<br>Tramadol  | Lowers seizure threshold; may be acceptable in patients with well-controlled seizures in whom alternative agents have not been effective  | Avoid   | Moderate  | Strong   |
| Delirium                          | All TCAs<br>Anticholinergics (see Table 9 for full list)<br>Benzodiazepines<br>Chlorpromazine<br>Corticosteroids<br>H <sub>2</sub> -receptor antagonist<br>Meperidine<br>Sedative hypnotics<br>Thioridazine | Avoid in older adults with or at high risk of delirium because of inducing or worsening delirium in older adults; if discontinuing drugs used chronically, taper to avoid withdrawal symptoms   | Avoid   | Moderate  | Strong   |
| Dementia and cognitive impairment | Anticholinergics (see Table 9 for full list)<br>Benzodiazepines<br>H <sub>2</sub> -receptor antagonists<br>Zolpidem<br>Antipsychotics, chronic and as-needed use  | Avoid because of adverse CNS effects. Avoid antipsychotics for behavioral problems of dementia unless nonpharmacological options have failed, and patient is a threat to themselves or others. Antipsychotics are associated with an increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia | Avoid   | High  | Strong   |
| History of falls or fractures     | Anticonvulsants<br>Antipsychotics<br>Benzodiazepines<br>Nonbenzodiazepine hypnotics<br>Eszopiclone<br>Zaleplon<br>Zolpidem<br>TCAs and selective serotonin reuptake inhibitors                              | Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls; shorter-acting benzodiazepines are not safer than long-acting ones   | Avoid unless safer alternatives are not available; avoid anticonvulsants except for seizure disorders | High  | Strong   |

(Continued)

Table 3. (Contd.)

| Disease or Syndrome     | Drug   | Rationale   | Recommendation                     | Quality of Evidence  | Strength of Recommendation |
|-------------------------|--|---|------------------------------------|--|----------------------------|
| Insomnia                | Oral decongestants<br>Pseudoephedrine<br>Phenylephrine   | CNS stimulant effects   | Avoid                              | Moderate   | Strong                     |
|                         | Stimulants<br>Amphetamine<br>Methylphenidate<br>Pemoline<br>Theobromines<br>Theophylline<br>Caffeine   |   |                                    |  |                            |
| Parkinson's disease     | All antipsychotics (see Table 8 for full list, except for quetiapine and clozapine)<br>Antiemetics<br>Metoclopramide<br>Prochlorperazine<br>Promethazine   | Dopamine receptor antagonists with potential to worsen parkinsonian symptoms. Quetiapine and clozapine appear to be less likely to precipitate worsening of Parkinson's disease               | Avoid                              | Moderate   | Strong                     |
| <i>Gastrointestinal</i> |  |   |                                    |  |                            |
| Chronic constipation    | Oral antimuscarinics for urinary incontinence<br>Darifenacin<br>Fesoterodine<br>Oxybutynin (oral)<br>Solifenacin<br>Tolterodine<br>Trospium<br>Nondihydropyridine CCB<br>Diltiazem<br>Verapamil<br>First-generation antihistamines as single agent or part of combination products<br>Brompheniramine (various)<br>Carbinoxamine<br>Chlorpheniramine<br>Clemastine (various)<br>Cyproheptadine<br>Dexbrompheniramine<br>Dexchlorpheniramine (various)<br>Diphenhydramine<br>Doxylamine<br>Hydroxyzine<br>Promethazine<br>Triprolidine<br>Anticholinergics and antispasmodics (see Table 9 for full list of drugs with strong anticholinergic properties)<br>Antipsychotics<br>Belladonna alkaloids<br>Clidinium-chlordiazepoxide<br>Dicyclomine<br>Hyoscyamine<br>Propantheline<br>Scopolamine<br>Tertiary TCAs (amitriptyline, clomipramine, doxepin, imipramine, and trimipramine) | Can worsen constipation; agents for urinary incontinence: antimuscarinics overall differ in incidence of constipation; response variable; consider alternative agent if constipation develops | Avoid unless no other alternatives | For urinary incontinence: high<br>All others:<br>Moderate to low | Weak                       |

(Continued)

Table 3. (Contd.)

| Disease or Syndrome  | Drug  | Rationale  | Recommendation   | Quality of Evidence                  | Strength of Recommendation                 |
|--|---|--|--|--------------------------------------|--|
| History of gastric or duodenal ulcers                      | Aspirin (>325 mg/d)<br>Non-COX-2 selective NSAIDs   | May exacerbate existing ulcers or cause new or additional ulcers | Avoid unless other alternatives are not effective and patient can take gastroprotective agent (proton pump inhibitor or misoprostol) | Moderate                             | Strong                                     |
| <i>Kidney and urinary tract</i>                            |   |  |  |                                      |  |
| Chronic kidney disease Stages IV and V                     | NSAIDs<br>Triamterene (alone or in combination)   | May increase risk of kidney injury                               | Avoid  | NSAIDs: moderate<br>Triamterene: low | NSAIDs: strong<br>Triamterene: weak        |
| Urinary incontinence (all types) in women                  | Estrogen oral and transdermal (excludes intravaginal estrogen)  | Aggravation of incontinence                                      | Avoid in women   | High                                 | Strong                                     |
| Lower urinary tract symptoms, benign prostatic hyperplasia | Inhaled anticholinergic agents<br>Strongly anticholinergic drugs, except antimuscarinics for urinary incontinence (see Table 9 for complete list) | May decrease urinary flow and cause urinary retention            | Avoid in men   | Moderate                             | Inhaled agents: strong<br>All others: weak |
| Stress or mixed urinary incontinence                       | Alpha blockers<br>Doxazosin<br>Prazosin<br>Terazosin  | Aggravation of incontinence                                      | Avoid in women   | Moderate                             | Strong                                     |

The primary target audience is the practicing clinician. The intentions of the criteria are to improve the selection of prescription drugs by clinicians and patients; evaluate patterns of drug use within populations; educate clinicians and patients on proper drug usage; and evaluate health-outcome, quality of care, cost, and utilization data.

CCB = calcium channel blocker; AChEI = acetylcholinesterase inhibitor; CNS = central nervous system; COX = cyclooxygenase; NSAID = nonsteroidal anti-inflammatory drug; TCA = tricyclic antidepressant.

Table 4 lists medications to be used with caution in older adults. Fourteen medications and classes were categorized. Two of these involve recently marketed anti-thrombotics for which early evidence suggests caution for use in adults aged 75 and older.

Table 5 is a summary of medications that were moved to another category or modified since the last update, and Tables 6 and 7 summarize medications that were removed or added since the last update. Nineteen medications and medication classes were dropped from the 2003 to the 2012 update of the criteria based on consensus of the panel and evidence or a rationale to justify their exclusion from the list. In several cases, medications were removed because they had been taken off the U.S. market since the 2003 update (e.g., propoxyphene) or because of insufficient or new evidence that was evaluated by the panel (e.g., ethacrynic acid). Table 8 includes a list of the antipsychotics included in the statements. Table 9 is the list of anticholinergic medications to be avoided in older adults compiled from drugs rated as having strong anticholinergic properties in the Anticholinergic Risk Scale,<sup>26</sup> Anticholinergic Drug Scale,<sup>27</sup> and Anticholinergic Burden Scale.<sup>28</sup>

## DISCUSSION

The 2012 AGS Beers Criteria is an important and improved update of previously established criteria widely

used by healthcare providers, educators, and policy-makers and as a quality measure. Previously, as many as 40% of older adults received one or more medications on this list, depending on the care setting.<sup>29–31</sup> The new criteria are based upon methods for determining best-practice guidelines that included a rigorous systematic literature review, the use of an expert consensus panel, and grading of the strength of evidence and recommendations.

The updated criteria should be viewed as a guideline for identifying medications for which the risks of their use in older adults outweigh the benefits. The medications that have a high risk of toxicity and adverse effects in older adults and limited effectiveness, and all medications in Table 2 (Independent of Diagnosis or Condition) should be avoided in favor of an alternative safer medication or a nondrug approach. The drug–disease or –syndrome interactions summarized in Table 3 are particularly important in the care of older adults because they often take multiple medications for multiple comorbidities. Their occurrence may have greater consequences in older adults because of age-related decline in physiological reserve. Recent studies in which drug–disease interactions have been shown to be important risk factors for ADEs highlight their importance.<sup>32</sup>

This list is not meant to supersede clinical judgment or an individual patient's values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making. The historical lack of

**Table 4. 2012 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution in Older Adults**

| Drug  | Rationale  | Recommendation   | Quality of Evidence | Strength of Recommendation |
|---|--|--|---------------------|----------------------------|
| Aspirin for primary prevention of cardiac events  | Lack of evidence of benefit versus risk in individuals aged $\geq 80$  | Use with caution in adults aged $\geq 80$                          | Low                 | Weak                       |
| Dabigatran  | Greater risk of bleeding than with warfarin in adults aged $\geq 75$ ; lack of evidence for efficacy and safety in individuals with CrCl $< 30$ mL/min   | Use with caution in adults aged $\geq 75$ or if CrCl $< 30$ mL/min | Moderate            | Weak                       |
| Prasugrel   | Greater risk of bleeding in older adults; risk may be offset by benefit in highest-risk older adults (e.g., with prior myocardial infarction or diabetes mellitus)   | Use with caution in adults aged $\geq 75$                          | Moderate            | Weak                       |
| Antipsychotics<br>Carbamazepine<br>Carboplatin<br>Cisplatin<br>Mirtazapine<br>Serotonin–norepinephrine reuptake inhibitor<br>Selective serotonin reuptake inhibitor<br>Tricyclic antidepressants<br>Vincristine | May exacerbate or cause syndrome of inappropriate antidiuretic hormone secretion or hyponatremia; need to monitor sodium level closely when starting or changing dosages in older adults due to increased risk | Use with caution   | Moderate            | Strong                     |
| Vasodilators  | May exacerbate episodes of syncope in individuals with history of syncope  | Use with caution   | Moderate            | Weak                       |

The primary target audience is the practicing clinician. The intentions of the criteria are to improve the selection of prescription drugs by clinicians and patients; evaluate patterns of drug use within populations; educate clinicians and patients on proper drug usage; and evaluate health-outcome, quality of care, cost, and utilization data.

CrCl = creatinine clearance.

**Table 5. Medications Moved to Another Category or Modified Since 2003 Beers Criteria**

| Independent of Diagnoses or Condition   | Considering Diagnoses   |
|---|---|
| Amphetamines (excluding methylphenidate hydrochloride and anorexics)                            | Fluoxetine, citalopram, fluvoxamine, paroxetine, and sertraline with syndrome of inappropriate antidiuretic hormone secretion |
| All barbiturates (except phenobarbital) except when used to control seizures                    | Olanzapine with obesity   |
| Naproxen, oxaprozin, and piroxicam  | Vasodilators with syncope   |
| Nitrofurantoin  |   |
| Non-cyclooxygenase selective nonsteroidal anti-inflammatory drugs (excludes topical)            |   |
| Oral short-acting dipyridamole; does not apply to the extended-release combination with aspirin |   |
| Oxybutynin  |   |
| Reserpine in doses $>0.25$ mg   |   |

inclusion of many older adults in drug trials<sup>33–35</sup> and the related lack of alternatives in some individual instances further complicate medication use in older adults. There may be cases in which the healthcare provider determines that a drug on the list is the only reasonable alternative (e.g., end-of-life or palliative care). The panel has attempted to evaluate the literature and best-practice guidelines to cover as many of these instances as possible, but not all possible clinical situations can be anticipated in such a broad undertaking. In these cases, the list can be used clinically not only for prescribing medications, but

also for monitoring their effects in older adults. If a provider is not able to find an alternative and chooses to continue to use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that ADEs can be incorporated into the electronic health record and prevented or detected early. These criteria also underscore the importance of using a team approach to prescribing, of the use of nonpharmacological approaches, and of having economic and organizational incentives for this type of model.

**Table 6. Medications Removed Since 2003 Beers Criteria**

| Independent of Diagnoses   | Considering Diagnoses   |
|--|---|
| Cimetidine (H <sub>2</sub> antihistamines added as a class; see Table 7)   | Antispasmodics and muscle relaxants; CNS stimulants: dextroamphetamine, methylphenidate, methamphetamine, pemoline, with cognitive impairment |
| Cyclandelate   | CNS stimulants: dextroamphetamine, methylphenidate, methamphetamine, pemoline, and fluoxetine with anorexia and malnutrition                  |
| Daily fluoxetine   | Clopidogrel with blood clotting disorders or receiving anticoagulant therapy  |
| Ferrous sulfate >325 mg/d  | Guanethidine with depression  |
| Guanadrel  | High-sodium content drugs with heart failure  |
| Guanethidine   | Monoamine oxidase inhibitors with insomnia  |
| Halazepam  | Oxybutynin and tolterodine with bladder outlet obstruction  |
| Long-term use of stimulant laxatives: bisacodyl, cascara sagrada, and neoloid except in the presence of opiate analgesic use | Pseudoephedrine and diet pills with hypertension  |
| Mesoridazine   | Tacrine with Parkinson's disease  |
| Propoxyphene and combination products  |   |
| Tripelennamine   |   |

CNS = central nervous system.

These criteria have some limitations. First, even though older adults are the largest consumers of medication, they are often underrepresented in drug trials.<sup>33,35</sup> Thus, using an evidence-based approach may underestimate some drug-related problems or lead to a weaker evidence grading. As stated previously, the intent of the updated 2012 AGS Beers Criteria, as an educational tool and quality measure, is to improve the care of older adults by reducing their exposure to PIMs. Second, it does not address other types of potential PIMs that are not unique to aging (e.g., dosing of primarily renally cleared medications, drug–drug interactions, therapeutic duplication). Third, it does not comprehensively address the needs of individuals receiving palliative and hospice care, in whom symptom control is often more important than avoiding the use of PIMs. Finally, the search strategies used might have missed some studies published in languages other than English and studies available in unpublished technical reports, white papers, or other “gray literature” sources.

Regardless, this update has many strengths, including the use of an evidence-based approach using the Institute of Medicine standards and the development of a partnership to regularly update the criteria. Thoughtful application of the criteria will allow for closer monitoring of drug use, application of real-time e-prescribing and interventions to decrease ADEs in older adults, and better patient outcomes. Regular updates will allow for the evidence for medications on the list to be assessed routinely, making it more relevant and sensitive to patient outcomes, with the goal of evaluating and managing drug use in older adults while considering the dynamic complexities of the health-care system.

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The following individuals were members of the AGS Panel to update the 2012 AGS Beers Criteria: Donna Fick, PhD, RN, FGSA, FAAN, School of Nursing and College of Medicine, Department of Psychiatry, Pennsylvania State

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Table 7. Medications Added Since 2003 Beers Criteria

| Independent of Diagnoses<br>Medication           | Considering Diagnoses                            |   |
|--|--|---|
|  | Corresponding Diagnosis or Syndrome              |   |
| Aspirin for primary prevention of cardiac events | Acetylcholinesterase inhibitors                  | Syncope   |
| Antiarrhythmic drugs, Class 1a, 1c, III          | Anticonvulsants                                  | History of falls or fractures                                 |
| Belladonna alkaloids                             | H <sub>1</sub> and H <sub>2</sub> antihistamines | Delirium  |
| Benztropine (oral)                               | Aspirin >325 mg                                  | History of gastric or duodenal ulcers                         |
| Brompheniramine                                  | Brompheniramine                                  | Chronic constipation  |
| Carbinoxamine                                    | Caffeine   | Insomnia  |
| Chloral hydrate                                  | Carbamazepine                                    | SIADH or hyponatremia   |
| Clemastine                                       | Carbinoxamine                                    | Chronic constipation  |
| Clomipramine                                     | Carboplatin                                      | SIADH or hyponatremia   |
| Clonazepam                                       | Clemastine (various)                             | Chronic constipation  |
| Dabigatran                                       | Clozapine  | Chronic seizures or epilepsy                                  |
| Desiccated thyroid                               | Cisplatin  | SIADH or hyponatremia   |
| Dexbrompheniramine                               | Cyclooxygenase-2 inhibitors                      | Heart failure   |
| Doxylamine                                       | Darifenacin                                      | Chronic constipation  |
| Dronedarone                                      | Desipramine                                      | Falls and fractures   |
| Estazolam  | Dexbrompheniramine                               | Chronic constipation  |
| Eszopiclone                                      | Dexchlorpheniramine                              | Chronic constipation  |
| First- and second-generation antipsychotics      | Doxylamine                                       | Chronic constipation  |
| Flurazepam                                       | Estrogen, transdermal                            | Urinary incontinence (all types) in women                     |
| Glyburide  | Eszopiclone                                      | History of falls or fractures                                 |
| Growth hormone                                   | Fesoterodine                                     | Chronic constipation  |
| Guanabenz  | Inhaled anticholinergics                         | Lower urinary tract symptoms and benign prostatic hyperplasia |
| Guanfacine                                       | Maprotiline                                      | Chronic seizures or epilepsy                                  |
| Insulin, sliding scale                           | Mirtazapine                                      | SIADH or hyponatremia   |
| Megestrol  | Nondihydropyridine calcium channel blockers      | Heart failure   |
| Metoclopramide                                   | Nortriptyline                                    | Falls and fractures   |
| Oral doxepin >6 mg/d                             | Pioglitazone                                     | Heart failure   |
| Phenobarbital                                    | Prochlorperazine                                 | Parkinson disease   |
| Prasugrel  | Rosiglitazone                                    | Heart failure   |
| Prazosin   | Scopolamine                                      | Chronic constipation  |
| Scopolamine                                      | Serotonin-norepinephrine reuptake inhibitors     | SIADH or hyponatremia   |
| Spirolactone                                     | Solifenacin                                      | Chronic constipation  |
| Testosterone                                     | Thiothixene                                      | Chronic seizures or epilepsy                                  |
| Trihexyphenidyl                                  | Thioridazine                                     | Syncope   |
| Trimipramine                                     | Triamterene                                      | Chronic kidney disease Stages IV and V                        |
| Tripolidine                                      | Tripolidine                                      | Chronic constipation  |
| Zaleplon   | Trospium   | Chronic constipation  |
| Zolpidem   | Vincristine                                      | SIADH or hyponatremia   |
|  | Zaleplon   | History of falls or fractures                                 |
|  | Zolpidem   | Dementia and cognitive impairment                             |

SIADH = syndrome of inappropriate antidiuretic hormone secretion.

Table 8. First- and Second-Generation Antipsychotics

| First-Generation<br>(Conventional) Agents | Second-Generation<br>(Atypical) Agents |
|---|--|
| Chlorpromazine                            | Aripiprazole                           |
| Fluphenazine                              | Asenapine                              |
| Haloperidol                               | Clozapine                              |
| Loxapine                                  | Iloperidone                            |
| Molindone                                 | Lurasidone                             |
| Perphenazine                              | Olanzapine                             |
| Pimozide                                  | Paliperidone                           |
| Promazine                                 | Quetiapine                             |
| Thioridazine                              | Risperidone                            |
| Thiothixene                               | Ziprasidone                            |
| Trifluoperazine                           |  |
| Triflupromazine                           |  |

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**Table 9. Drugs with Strong Anticholinergic Properties**

|  |                      |                           |
|--|----------------------|---------------------------|
| Antihistamines                         | Antiparkinson agents | Skeletal Muscle Relaxants |
| Brompheniramine                        | Benztropine          | Carisoprodol              |
| Carbinoxamine                          | Trihexyphenidyl      | Cyclobenzaprine           |
| Chlorpheniramine                       |                      | Orphenadrine              |
| Clemastine                             |                      | Tizanidine                |
| Cyproheptadine                         |                      |                           |
| Dimenhydrinate                         |                      |                           |
| Diphenhydramine                        |                      |                           |
| Hydroxyzine                            |                      |                           |
| Loratadine                             |                      |                           |
| Meclizine                              |                      |                           |
| Antidepressants                        | Antipsychotics       |                           |
| Amitriptyline                          | Chlorpromazine       |                           |
| Amoxapine                              | Clozapine            |                           |
| Clomipramine                           | Fluphenazine         |                           |
| Desipramine                            | Loxapine             |                           |
| Doxepin                                | Olanzapine           |                           |
| Imipramine                             | Perphenazine         |                           |
| Nortriptyline                          | Pimozide             |                           |
| Paroxetine                             | Prochlorperazine     |                           |
| Protriptyline                          | Promethazine         |                           |
| Trimipramine                           | Thioridazine         |                           |
|  | Thiothixene          |                           |
|  | Trifluoperazine      |                           |
| Antimuscarinics (urinary incontinence) | Antispasmodics       |                           |
| Darifenacin                            | Atropine products    |                           |
| Fesoterodine                           | Belladonna alkaloids |                           |
| Flavoxate                              | Dicyclomine          |                           |
| Oxybutynin                             | Homatropine          |                           |
| Solifenacin                            | Hyoscyamine products |                           |
| Tolterodine                            | Propantheline        |                           |
| Trospium                               | Scopolamine          |                           |

America; National Academies of Practice, Academy of Pharmacy; National Committee for Quality Assurance; Pharmacy Quality Alliance; Society for General Internal Medicine; Society of Hospital Medicine.

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